Beyond Old Debates: New Systems Risk Analysis (NESRA) in An Action-oriented Approach

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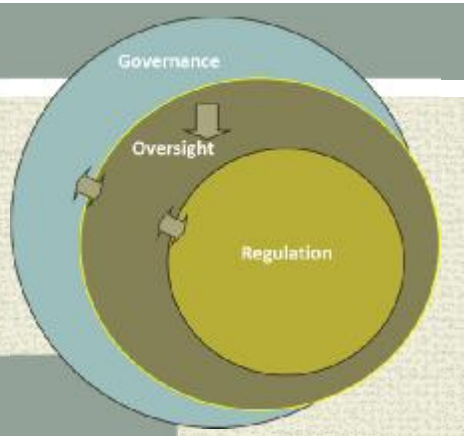
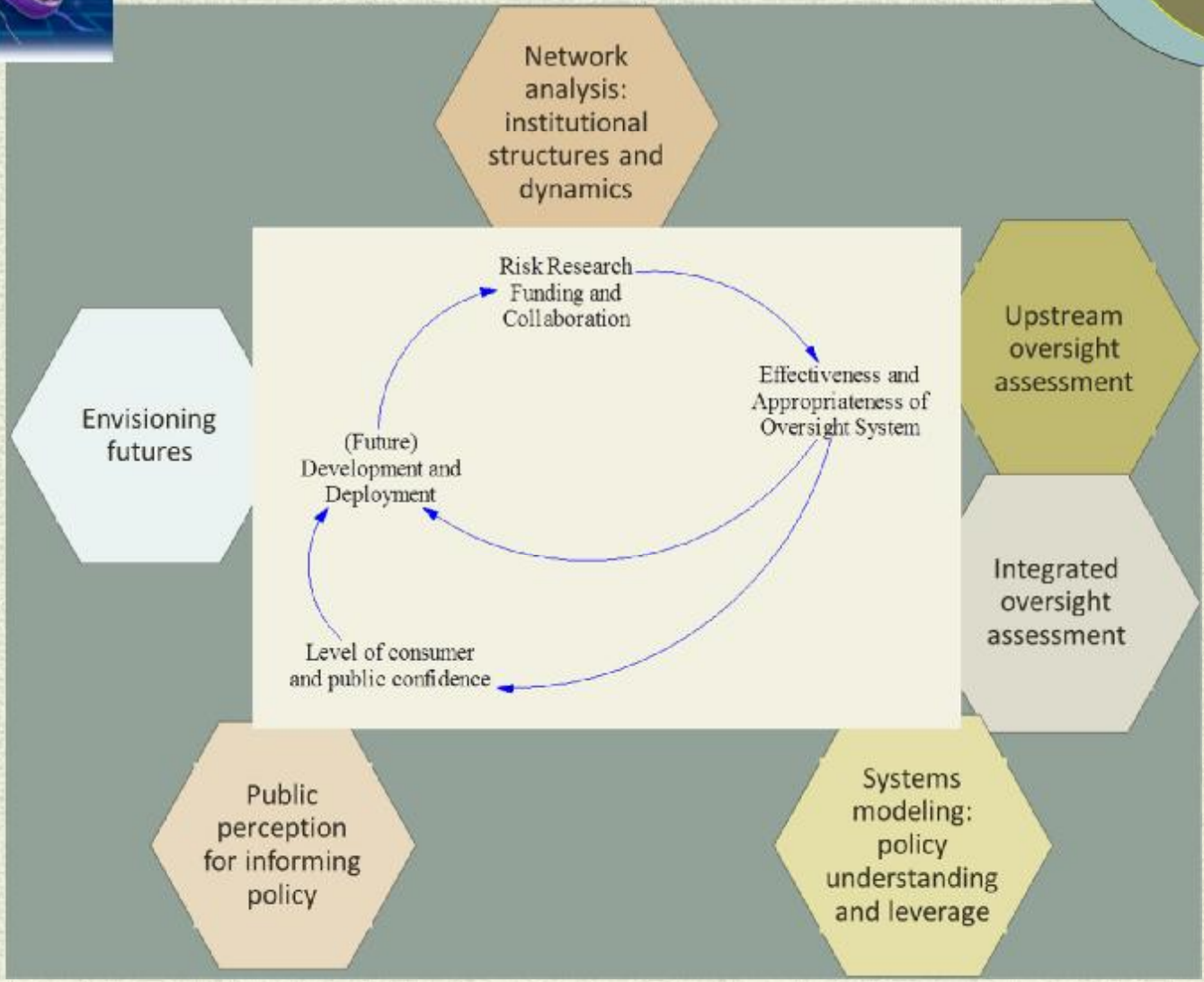
NAS Forum on Understanding Risk Frameworks for Synthetic Biology
March 13, 2014

Outline

- Broader areas of governance research
- Premises
- New Systems Risk Analysis (NeSRA)
- Action-Oriented Governance (A-OG)
- Policy Context

Emerging Technologies and Governance Systems





Research Projects

- **USDA Food Policy Research Center grant**
- *Public Perceptions of GM and nano food: benefits, labeling, and adoption (national survey)*

- **NSF grant--DBI**
- *Plant genome editing: societal role and implications for Governance*
  - Stakeholder attitudes and bibliometric analysis

- **Sloan Foundation Grant**
- *Governance for Emerging Cases of Synthetic Biology*

- **NSF-NNIN Grant**
- *Definitions of Nanotechnology among Expert Groups*

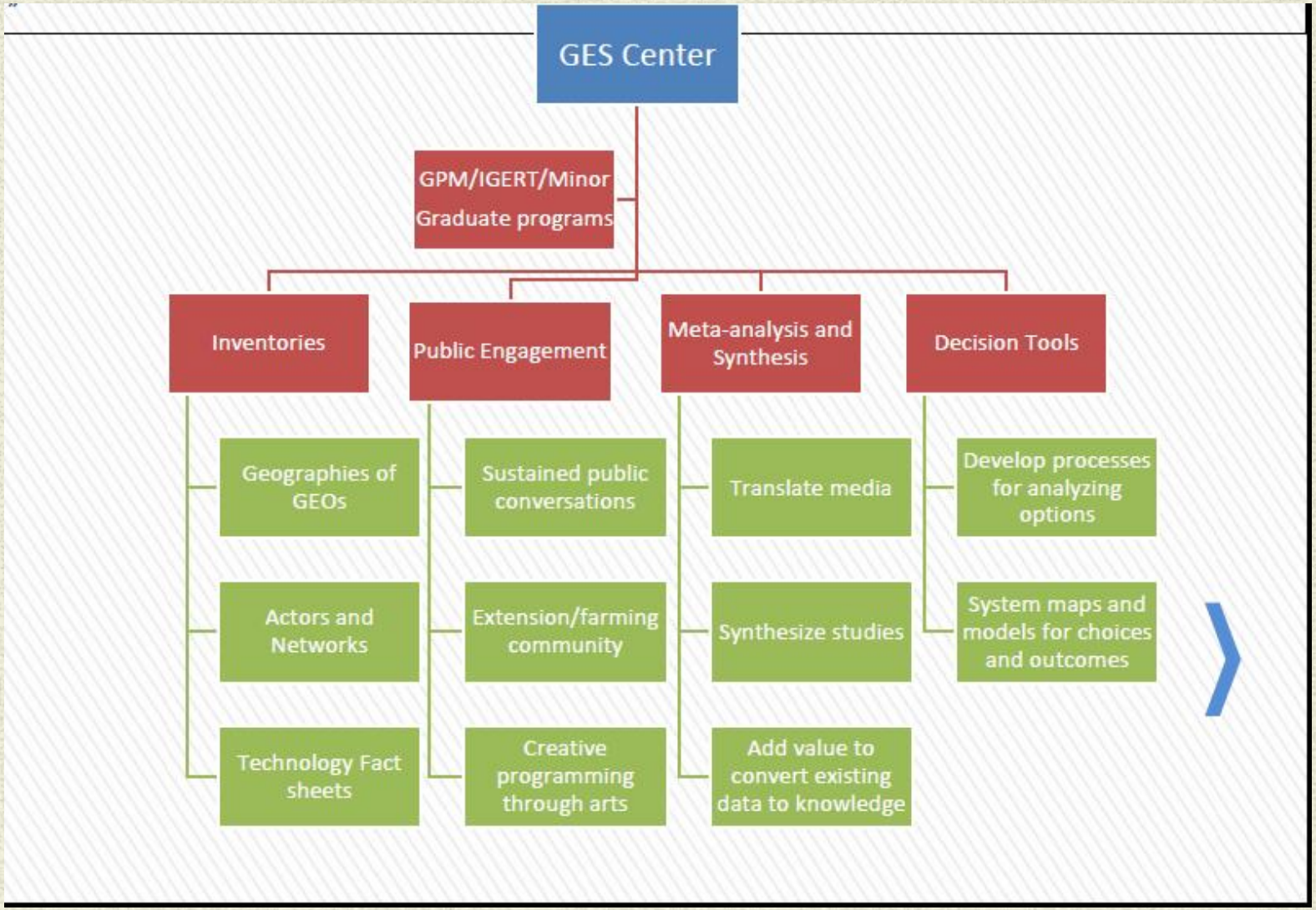
- **NSF grant—SciSip/ST&S**
- *Women in Science and Technology Policy*

- **NSF grant—ST&S**
- *Evaluating Oversight Models for Nano-biotechnology*

- *Co-Director of the Center for Genetic Engineering and Society*

NC STATE UNIVERSITY

Center for
Genetic Engineering & Society



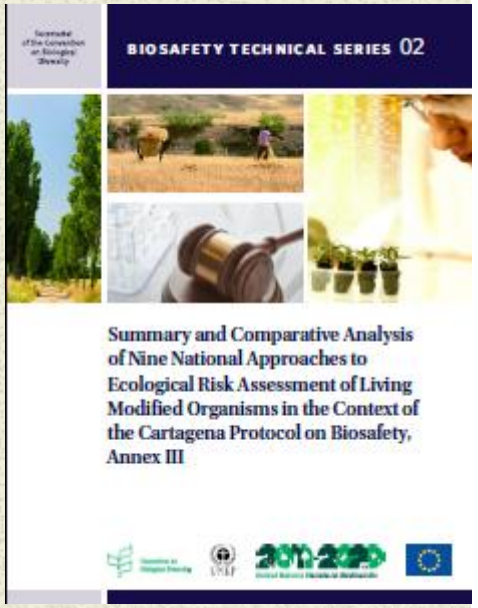
NSF IGERT Ph.D. Minor Program(s)

U of MN—Risk Analysis for Introduced Species and Genotypes

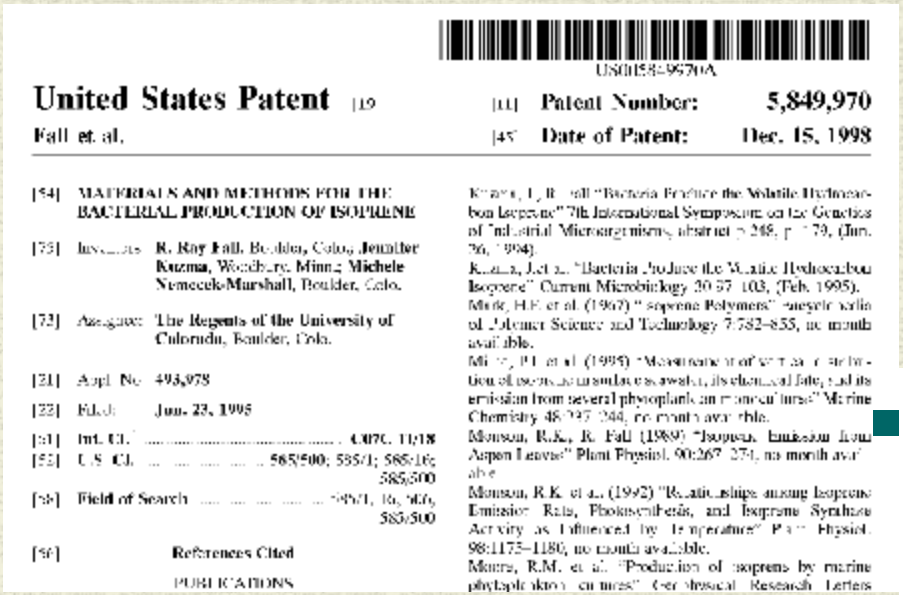
Report for UN-CBD-Biosafety Protocol

NCSU- Genetic Pest Management

- 1st Cohort—2012-2013
  - GM mosquitos for Dengue (Peru)
- 2nd Cohort—2013-2014
  - GM rodents for invasive species (Channel Islands, CA)
- 3rd Cohort—2014-2015
  - GM pests for agricultural pest control (Mexico)



A Checkered Past…



US005849970A

United States Patent [19]

Fall et al.

[11] **Patent Number: 5,849,970**

[45] **Date of Patent: Dec. 15, 1998**

[54] MATERIALS AND METHODS FOR THE BACTERIAL PRODUCTION OF ISOPRENE

[75] Inventors: R. Ray Fall, Boulder, Colo.; Jennifer Kuzma, Woodbury, Minn.; Michele Nemecek-Marshall, Boulder, Colo.

[73] Assignee: The Regents of the University of Colorado, Boulder, Colo.

[21] Appl. No.: 493,978

[22] Filed: Jun. 23, 1995

[51] Int. Cl. C07C 11/18

[52] U.S. Cl. 585/500; 585/1; 585/16; 585/500

[58] Field of Search 585/1, 16, 500, 585/500

[56] References Cited

PUBLICATIONS

Kuzma, J. et al. "Bacteria Produce the Volatile Hydrocarbon Isoprene" 7th International Symposium on the Genetics of Industrial Microorganisms, abstract p 248, p 179, (Jun. 26, 1994).

Kuzma, J. et al. "Bacteria Produce the Volatile Hydrocarbon Isoprene" Current Microbiology 30:97-103, (Feb. 1995).

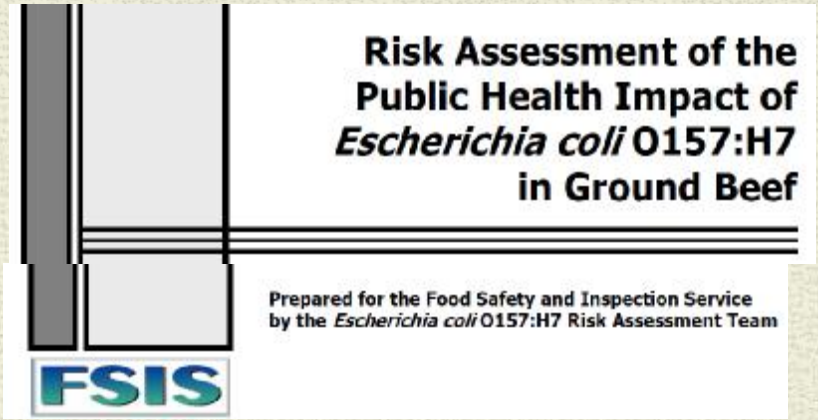
Morris, H.F. et al. (1967) "Isoprene Polymers" Enzymic xylitol Polymer Science and Technology 7:782-855, no month available.

Mi[illegible], P.I. et al. (1995) "Measurement of [illegible] Gaseous Isoprene in Surface Seawater, its Chemical Fate, and its emission from several phytoplankton monocultures" Marine Chemistry 48:237-244, no month available.

Monson, R.K., R. Fall (1989) "Isoprene Emission from Aspen Leaves" Plant Physiol. 90:267-274, no month available

Monson, R.K. et al., (1992) "Relationships among Isoprene Emission Rate, Photosynthesis, and Isoprene Synthase Activity as Influenced by Temperature" Plant Physiol. 98:1175-1180, no month available.

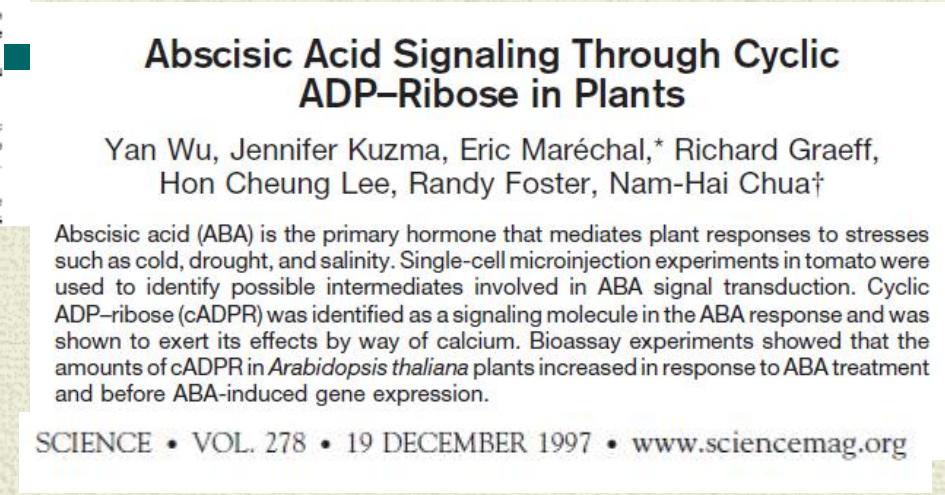
Morris, R.M. et al. "Production of Isoprene by marine phytoplankton cultures" Geophysical Research Letters



Risk Assessment of the Public Health Impact of *Escherichia coli* O157:H7 in Ground Beef

Prepared for the Food Safety and Inspection Service by the *Escherichia coli* O157:H7 Risk Assessment Team

FSIS



Abscisic Acid Signaling Through Cyclic ADP–Ribose in Plants

Yan Wu, Jennifer Kuzma, Eric Maréchal,* Richard Graeff, Hon Cheung Lee, Randy Foster, Nam-Hai Chua†

Abscisic acid (ABA) is the primary hormone that mediates plant responses to stresses such as cold, drought, and salinity. Single-cell microinjection experiments in tomato were used to identify possible intermediates involved in ABA signal transduction. Cyclic ADP–ribose (cADPR) was identified as a signaling molecule in the ABA response and was shown to exert its effects by way of calcium. Bioassay experiments showed that the amounts of cADPR in *Arabidopsis thaliana* plants increased in response to ABA treatment and before ABA-induced gene expression.

SCIENCE • VOL. 278 • 19 DECEMBER 1997 • www.sciencemag.org

Focus on nexus of RA and governance (oversimplification)

Starting premises—
Considering broader harms lead to better scientific understanding

- Different types of harms that need to be considered in risk analysis
- Otherwise, it is NOT a science-based process
- Science acknowledges these types of harms and damages that can occur with “exposure”
  - 1st order physical health and environmental
  - 2nd order physical health and environmental
  - Social structure harm
  - Ethical affronts (without choice, voice, or consent)
  - Psychological well-being
  - Financial impacts (direct)
  - Economic impacts (indirect)
  - Cultural disruption

Risk Perspectives (O. Renn)

Figure 3.1
A Systematic Classification of Risk Perspectives

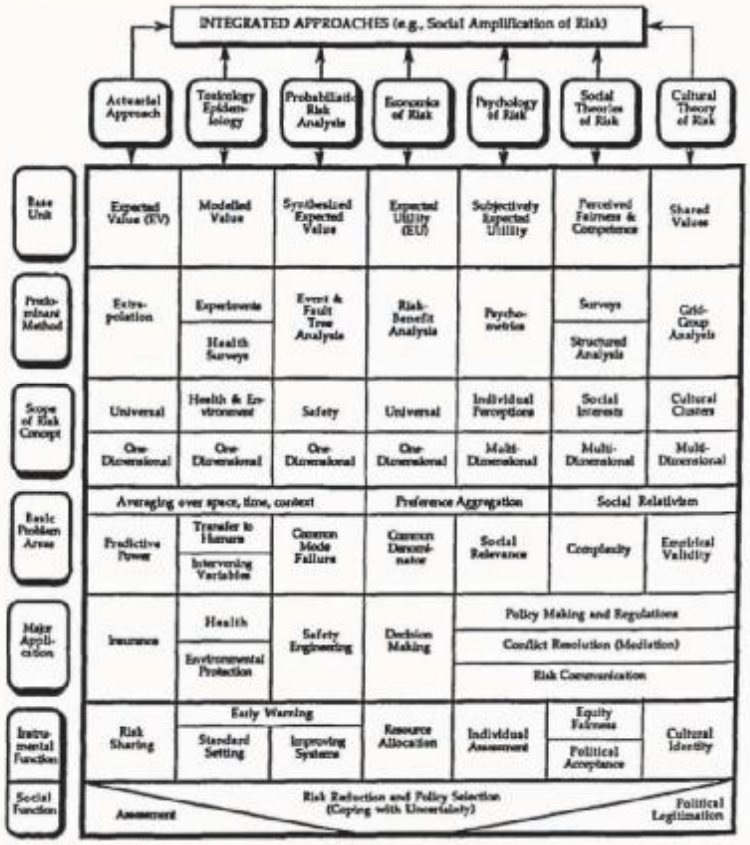
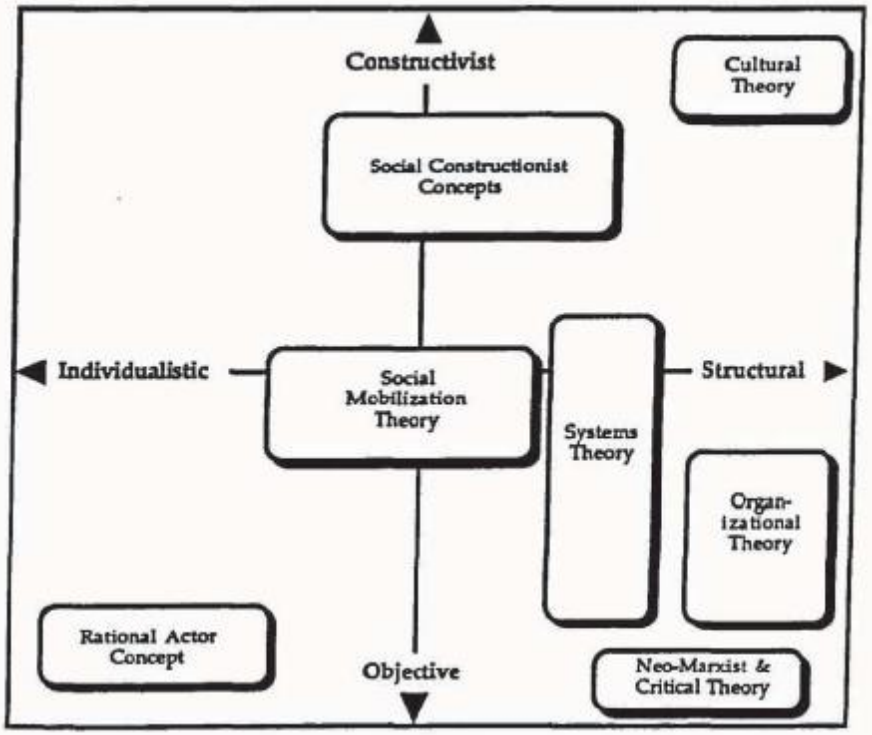
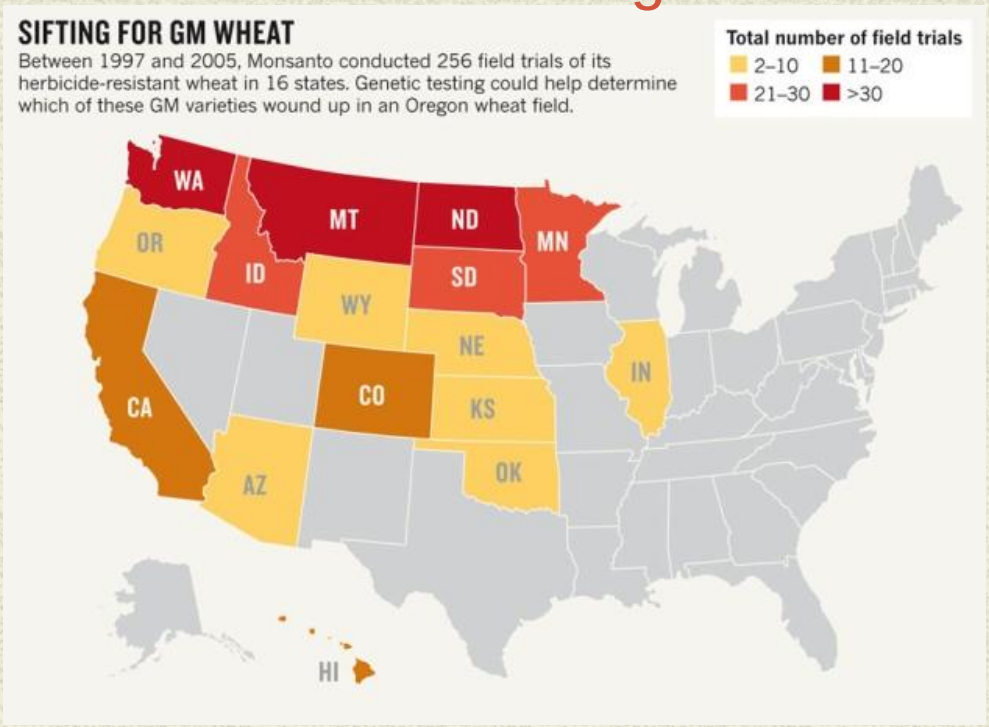


Figure 3.2
Major Sociological Perspectives on Risk



GM Wheat--Growing tension



GM soy Brazil -3-4x RR herbicide, paraquat use increasing.

Did we learn? Why not?

- Kuzma, J. in ***Innovative Governance Models for Emerging Technologies*** Eds. Marchant, Abbott, & Allenby. Edward Elgar (2014)

Revolution (2010-present)

- (2010) USDA decides not to exert authority for Zinc Finger Nuclease low phytate corn
- (2011) In January, Congress has hearing about GE alfalfa case. Several members of Congress question USDA's authority under the PPA to regulate GM crops at all.
- (2011) After completing the HT alfalfa EIS, USDA decides to fully deregulate HT alfalfa allowing for its unrestricted use.
- (2011) While in the process of completing the EIS for HT sugar beets, USDA partially deregulates them allowing for their restricted commercial use
- (2011) USDA approves amylase corn without EIS
- (2011-2012) USDA deregulates several GE crops without EIS

Including HT grass without any regulatory review…

Old debates force “old risk analysis”

- “Science-based” vs. Value based
- Substantially novel vs. substantially equivalent
- (compared to GM, conventionally reproduced)
- Blind Bans vs. Blind Promotion
- No governance vs. Command & Control governance
- Hope for humankind vs. planetary disaster

- Force inaction—
  - Either inappropriate approvals (GM Ht Bentgrass)
  - Significant delays on decisions (Golden Rice, GM Salmon)

- Not good for “market” or “public” success
  - (Bozeman and Sarewitz 2002)

Technological understandings—is it new?

- Synthetic biology is both incremental and exponential
- Continuum of approaches from regular GE to artificial life

Regulation & Governance (2010) 4, 92–112 doi:10.1111/j.1748-5991.2010.01071.x

Unpackaging synthetic biology: Identification of oversight policy problems and options

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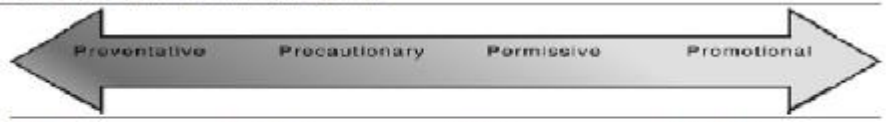
Todd Tanji
MS Program in Science, Technology, and Environmental Policy, Humphrey Institute of Public Affairs, University of Minnesota, Minneapolis, MN, USA

Table 2 Broad oversight policy options for synthetic biology (SB) applications



	Preventative	Precautionary	Permissive	Promotional
Intellectual property	No access to information	Highly restricted access to information	Largely open access to information	Open access to information
Biosecurity	Control of information and tools by a few	Several have control of information and tools	Most have control of information and tools	Unrestricted access to information and tools
Biosafety	Ban on usage of SB products	Stringent, mandatory government regulation of environmental health and safety	Voluntary or flexible mandatory programs and standards for environmental health and safety	No specific SB provisions or standards for environmental health and safety
Ethics	Ban SB applications with moral objections	Widespread dialogue and deliberation before SB is deployed	Transparent decisionmaking with input from various non-expert stakeholders	Closed processes with little input outside of SB scientific community and decisionmakers
Treatment of SB applications				
	Preventative	Precautiona	Permissive	Promotional
	Highly engineered living cells or systems in food and agriculture and environment Artificial living cells or systems in food and agriculture and environment	Highly engineered living cells or systems in medicine and consumer products Artificial living cells or systems in medicine and consumer products	Systems of non-living biological parts (all sectors) Highly engineered living cells or systems in chemical synthesis or energy Artificial living cells or systems in chemical synthesis or energy	Non-living biological parts (all sectors)

- Typology: Product Sectors and Technologies of SB
- Not definitive, but argues for case study approach
- Most funded projects now are using such an approach (Sloan, NSF)

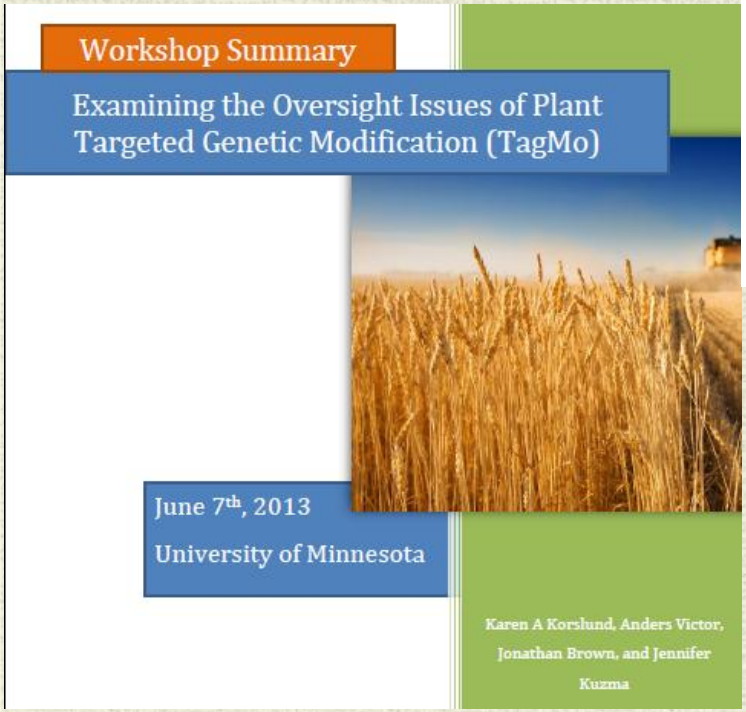
- First case study of ours: Plant Genome Editing using ZFN, TALENs—to explore transition towards SB & governance needs

Must it be brand new always?

I argue…

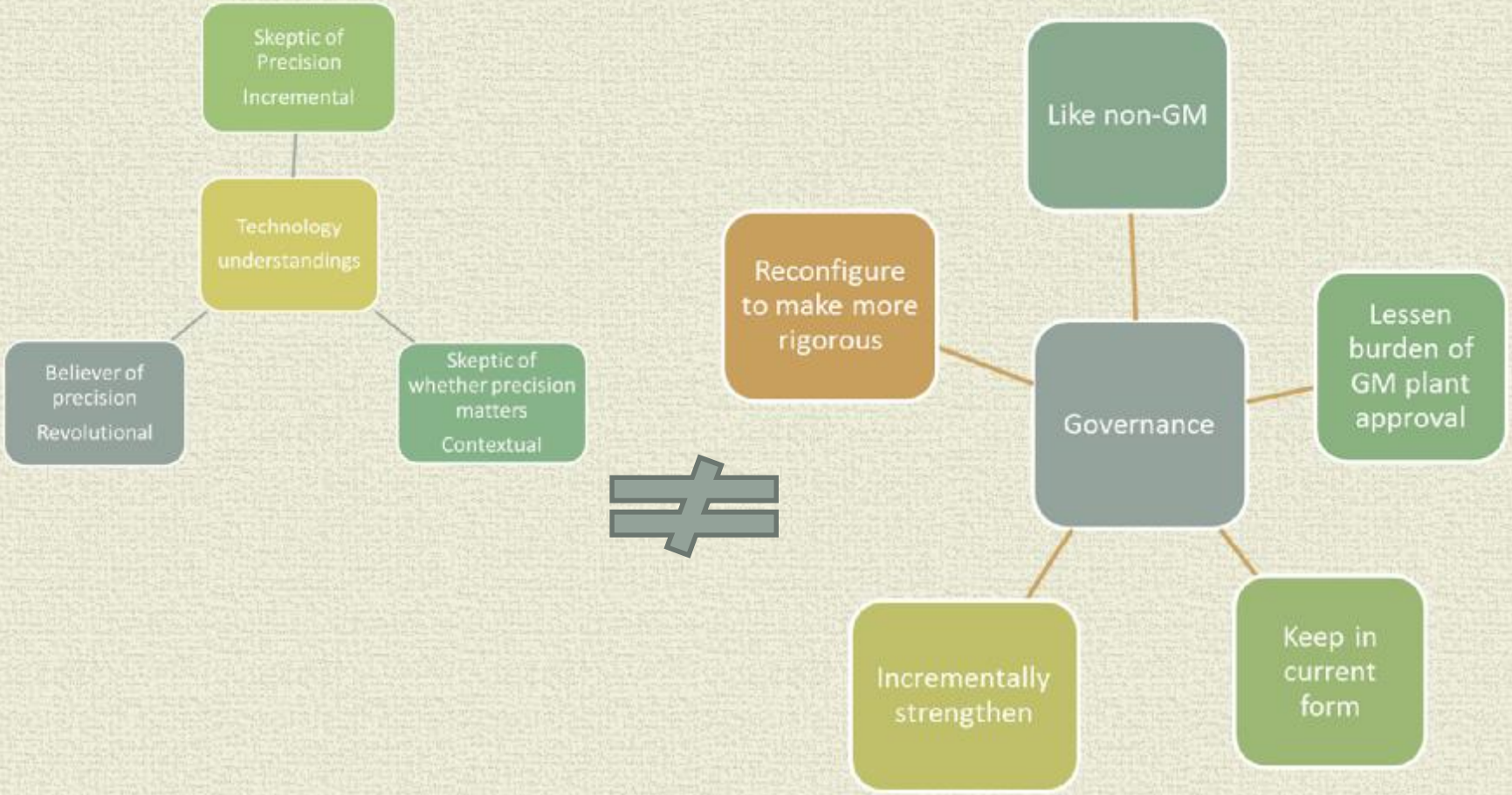
- Need for oversight is NOT dependent on the presentation of unique risk categories or absolute novelty of the technologies
  - If a technological component is novel enough to enough to patent. Should it be considered novel enough to be captured in a pre-release/market review process?
  - What happens after that is a matter for “new systems risk analysis” (e.g. voluntary standard setting or mandatory safety studies, field and clinical trials)

Genome Editing & Governance
(NSF funded—working with ZFN-TALEN developers



Genome Editing Interviews:

- "Scientific" understandings of technology are diverse
- how can oversight be based solely on whether technology is "new" or not?
- Technology understandings of SMEs do not map neatly onto governance policy preferences



Complex, Uncertain System

- "As we're able to…have **more and more powerful techniques** to modify these plants, we will be able to modify these plants more and more from their standard configurations. Especially with gene addition, we can **completely rewire a number of these plants**… The one concern I have is that if we're creating plants **before we really know what the sorts of products are."**
  - *- Genome editing researcher*

All you've done is taken a few bases out, **which fundamentally changed the physiology**, but there's no clear regulatory pathway by which that plant would or would not be considered genetically modified. So I think we'll probably see **significantly streamlined approval processes**. And actually, **one thing that we're hoping for as a business is that the regulatory hurdles will actually be raised for GM plants that are not made using technologies like ours**."

Genome editing researcher

Narratives of governance change

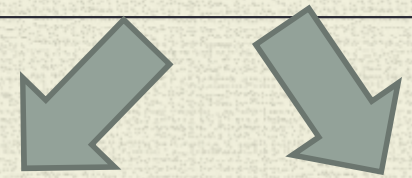
TagMo is an Incremental Technology --

- Maybe TagMo doesn't change technology concerns dramatically
- It doesn't FORCE a governance change, but gives us OPPORTUNITY to re-examine and change governance.

Opportunist

TagMo is Revolutionary Technology

- TagMo is a dramatically different technology that forces a change in governance: How?



Relaxes need for oversight

Hype-Hypo

Intensifies need for oversight

Systems context

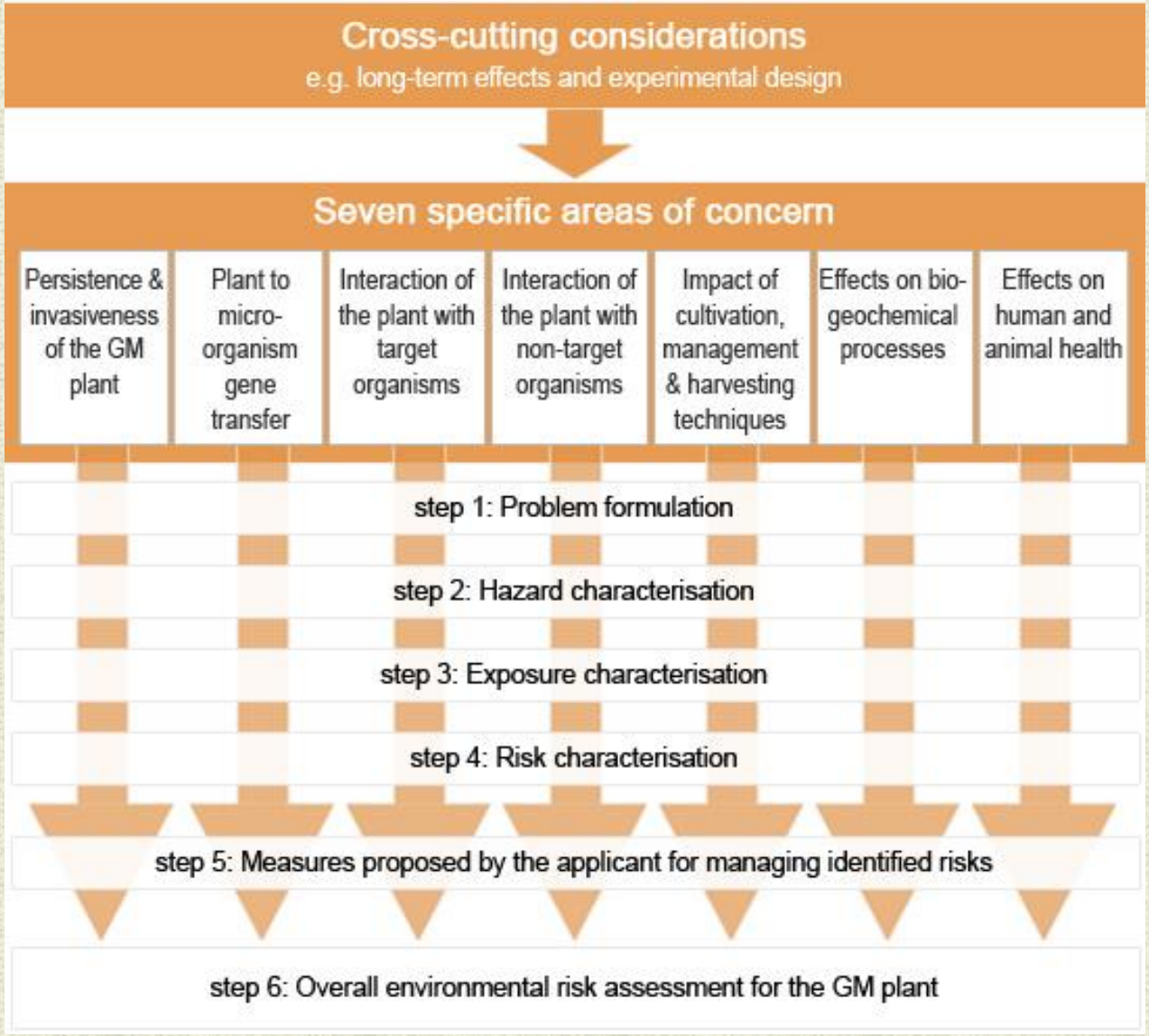
Need for Innovation in "new systems risk analysis" to Match Technological innovation

- It's better science,
- Social, policy, organization, behavioral, ecological science and relationships to health, happiness, and well-being.
- I don't know what the paradigm shift should be exactly. But the following are some proposals.
  - New Systems Risk Analysis (NeSRA)
  - Action-Oriented Governance (A-OG)

Consider open systems for “new systems risk analysis” (NeSRA)

- More scientific
  - the world is not linear, technologies are not closed off from it
- Consider RA in broader systems context
  - including benefits, alternatives, secondary impacts, just distribution, which are empirically linked to direct risks in systems.
- Unexpected consequences of complex systems are to be expected
  - (based on historical evidence),
- Foresight exercises and monitoring should attempt to reveal them.
- Best conducted with multiple and diverse “*interested and affected parties”*
  - (NRC 1996)
- *Risk analysis process becomes more scientific, and objective in light of the above*
  - *(“strong objectivity” S. Harding)*

LCRA—A little broader…but not there yet..
(EFSA GM crop RA)



Strategic Environmental Assessment—SES concerns (U.S. is falling behind)

Meyer *Environmental Sciences Europe* 2011, **23**:7
http://www.enveurope.com/content/23/1/7

Environmental Sciences Europe
a SpringerOpen Journal

REVIEW **Open Access**

Systemic risks of genetically modified crops: the need for new approaches to risk assessment

Hartmut Meyer

Abstract

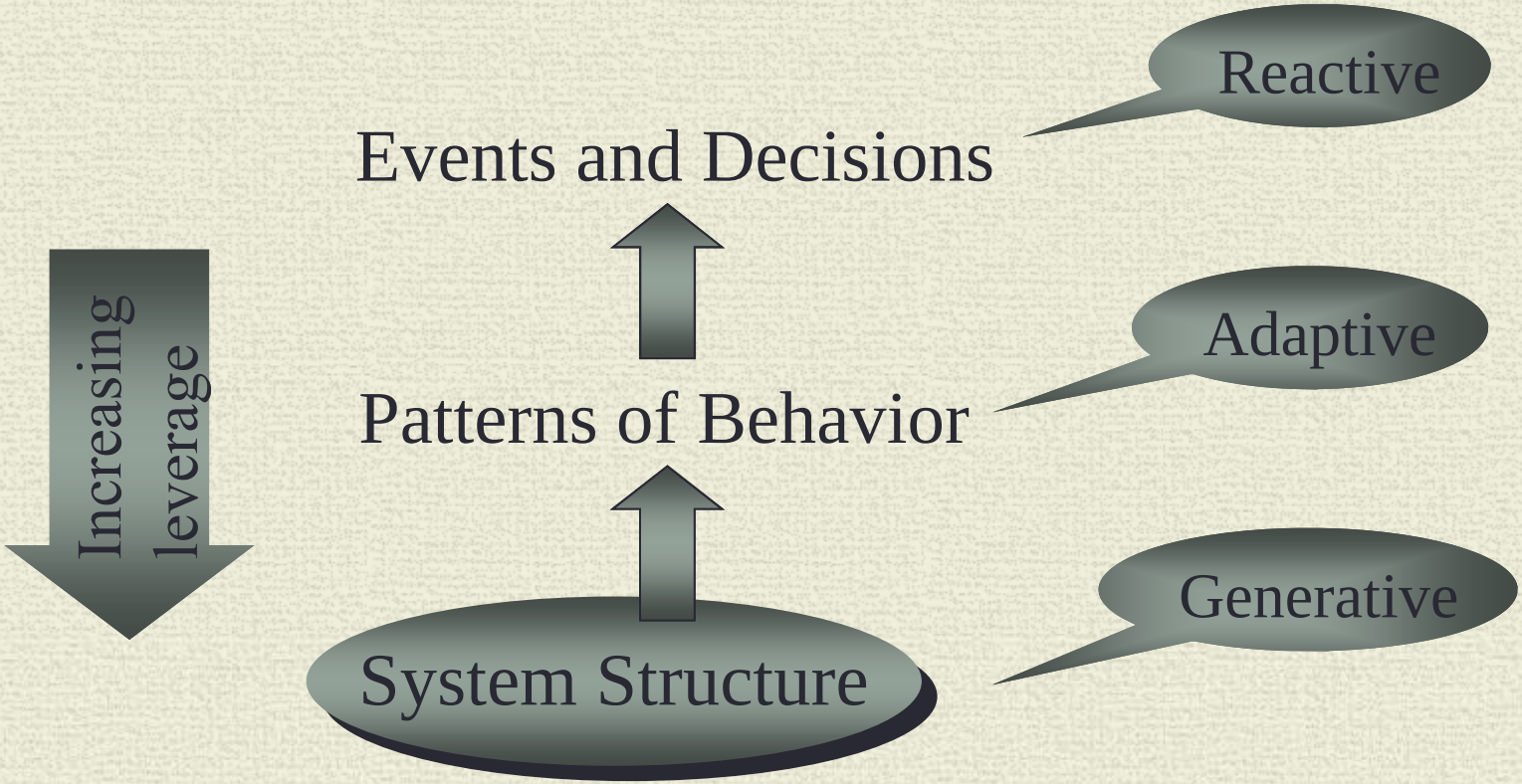
Purpose: Since more than 25 years, public dialogues, expert consultations and scientific publications have concluded that a comprehensive assessment of the implications of genetic engineering in agriculture and food production needs to include health, environmental, social and economical aspects, but only very few legal frameworks allow to assess the two latter aspects. This article aims to explain the divergence between societal debate and biosafety legislation and presents approaches to bring both together.

Main features: The article reviews the development of biosafety regulations in the USA and the EU, focussing on diverging concepts applied for assessing the risks of genetically modified organisms (GMOs).

Results: The dominant environmental risk assessment methodology has been developed to answer basic questions to enable expedient decision making. As a first step, methodologies that take into account complex environmental and landscape aspects should be applied. Expanding the scope of risk assessment, more holistic concepts have been developed, for example the Organisation for Econonomic Co-operation and Development (OECD) concept of systemic risks which includes socio-economic aspects. International bodies as the OECD, the Convention on Biological Diversity (CBD) and the European Union (EU) have developed the Strategic Environmental Assessment (SEA) as an instrument that includes the additional aspects of risk assessment as demanded by many stakeholders. Interestingly, there had been no attempts yet to link the existing frameworks of GMO risk assessment and SEA.

Conclusions: It is recommended to adapt current models of SEA to assess the systemic risks of GMOs. It is also suggested to revise the EU GMO legislation to promote the inclusion of SEA elements.

The Systems Perspective



Adapted from G. Richardson, U of Albany

Inaction or Action in face of little information of data?

Forrester 1991

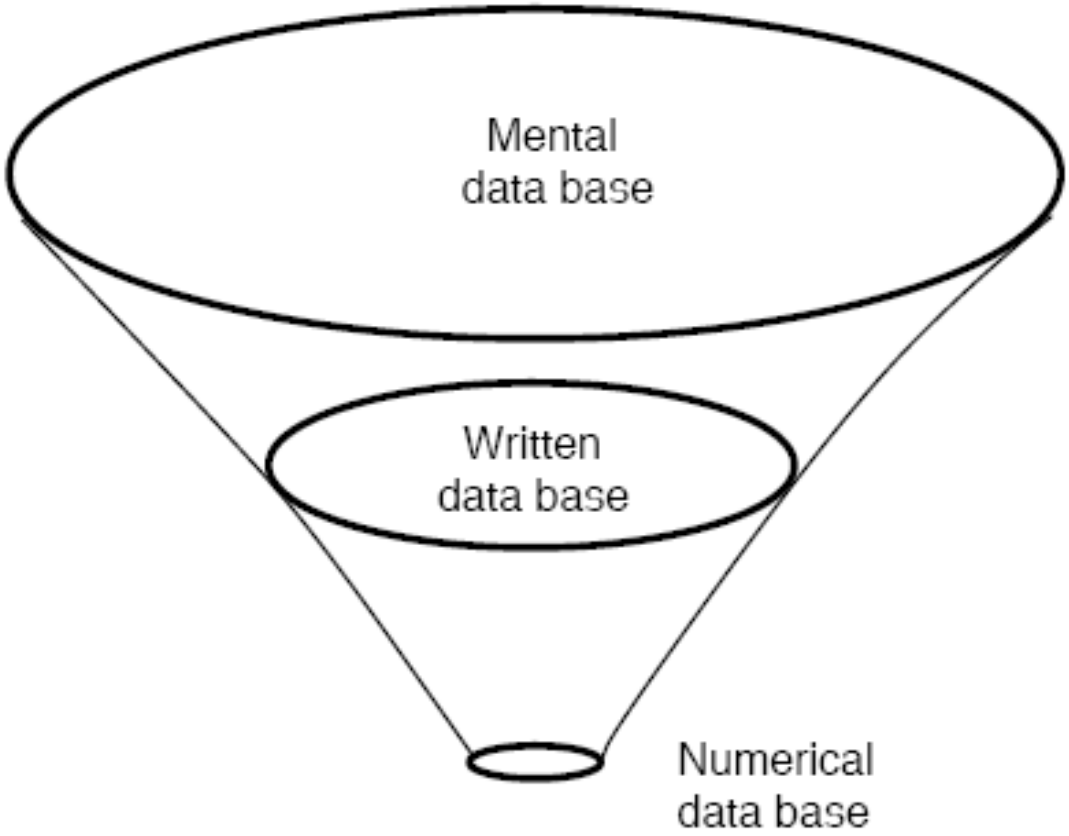


Figure 4. Decreasing information content in moving from mental to written to numerical data bases.

Limits to Growth,

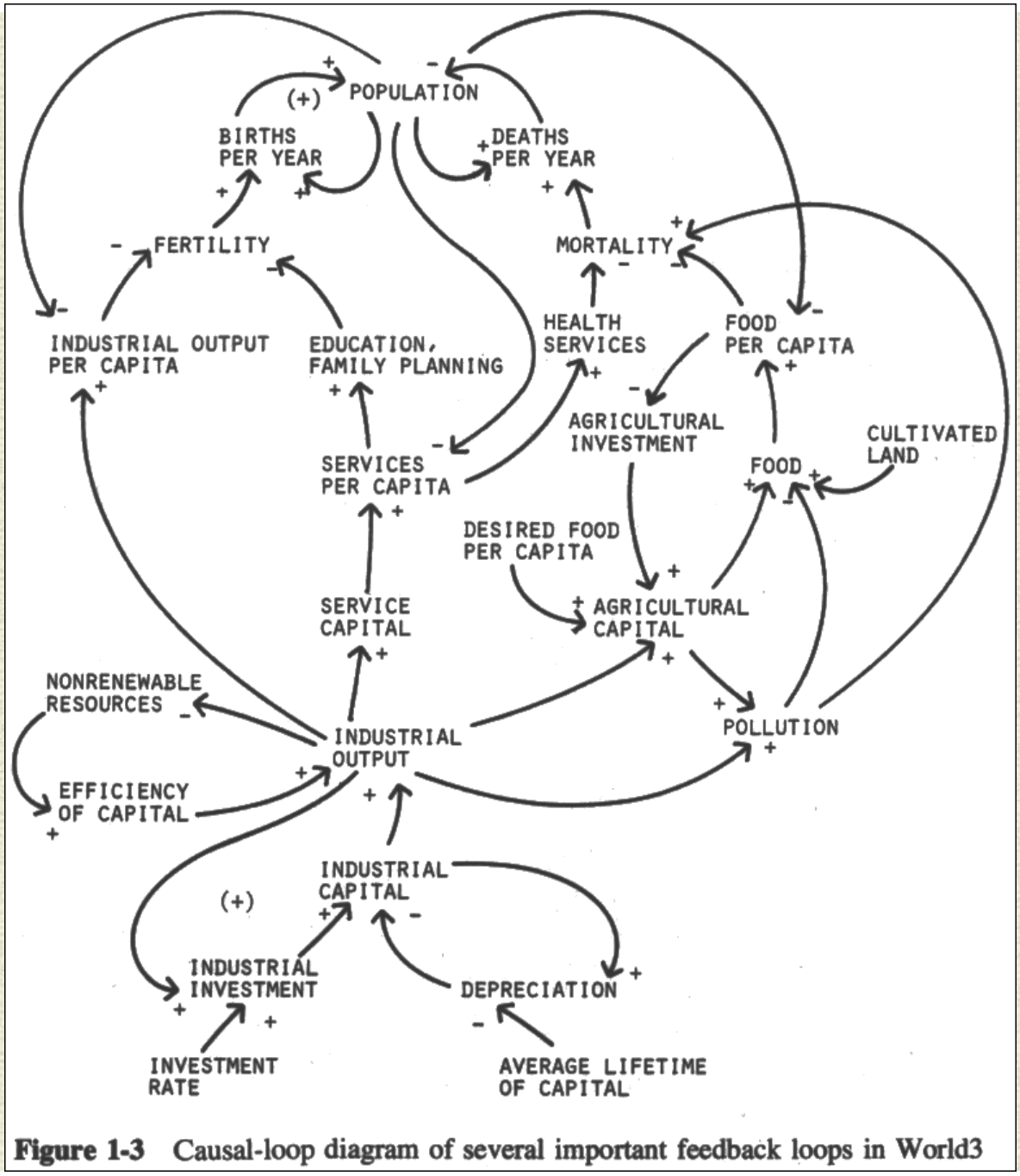


Figure 1-3 Causal-loop diagram of several important feedback loops in World3

Future Studies (Cornish)

The Problems of Progress

In general, what we call "progress" can lead to abuse of the natural environment, the burden of learning new jobs, and general disorientation due to change itself. Examples of other negative consequences of "progress":

Better machines	→	Displaced workers, loss of status
Growing wealth	→	Increase in rich/poor disparity, fewer workers for less-desired tasks
New products	→	Difficulty of making choices
More, better food	→	Obesity, clogged arteries
Better health care	→	Rising costs, higher expectations
Longer lives	→	Cost of supporting idle elderly, increase in disability, stress on natural resources
Saving newborn	→	More birth defects
Better transport	→	Decline of local communities
More TV programs	→	Inactivity, desocialization
Increasing comfort	→	Boredom, apathy
Portable telephones	→	Forced exposure to noxious chatter
Easy bill paying	→	Credit-card fraud, identity theft
Quick information	→	Internet hoaxes, scams, viruses
Cheap, easy messaging	→	Junk e-mail, insensitive comments

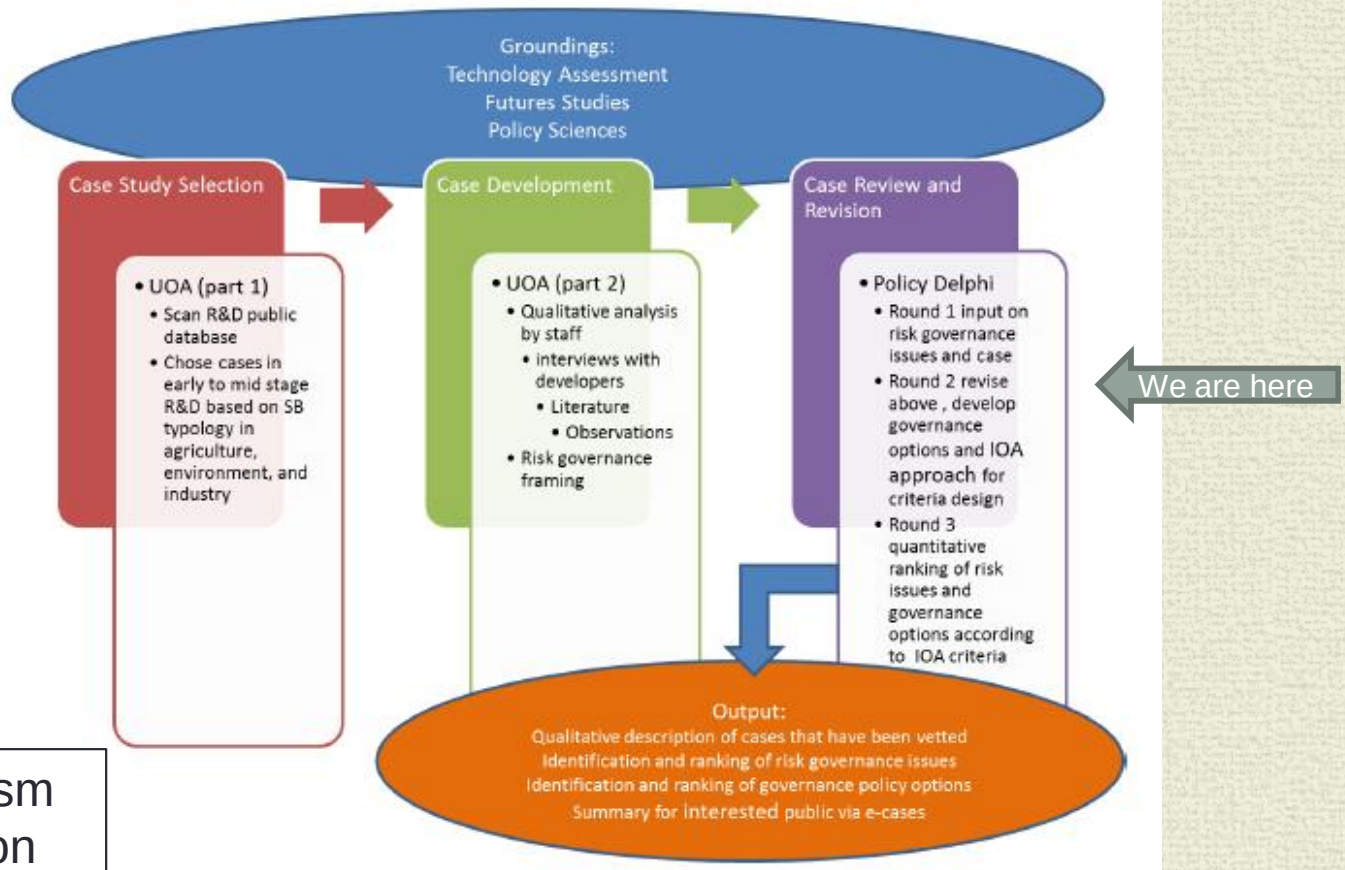
Future Studies Methods (Bell 1994)

- Correlations—variable predictions
- Time series extrapolation
- Survey Research
- The Delphi Method (policy Delphi, Turnoff)
- Simulation Modeling
- Gaming
- Monitoring
- Content Analysis
- Participatory Futures Praxis
- Social Experiments
- Ethnographic Research
- Etc.

Policy Delphi
Could be a starting point for more action-oriented approach

Kuzma PI, Cummings co-PI 2013-2014
Sloan Foundation SB Program

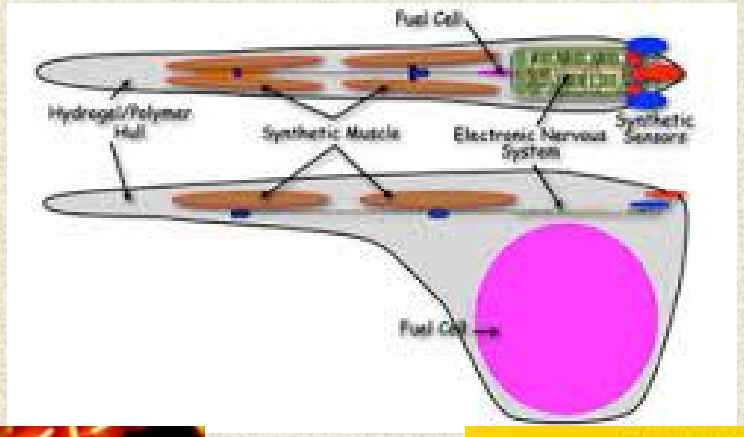
Figure 1. Overall Methodology and Theoretical Framework

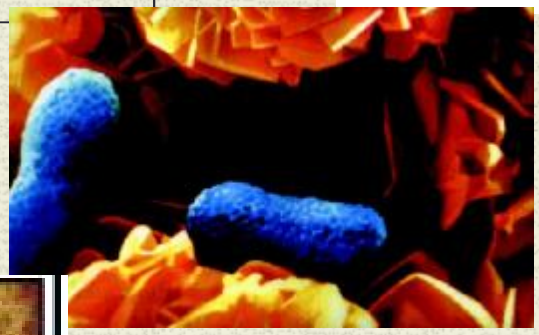


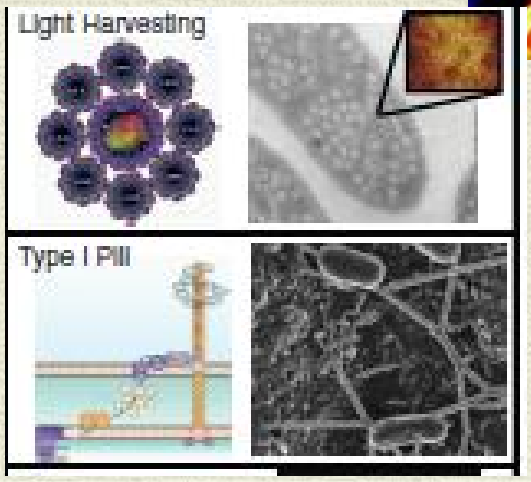
Cyberplasm
Dextinction
Biomining
N-fixation

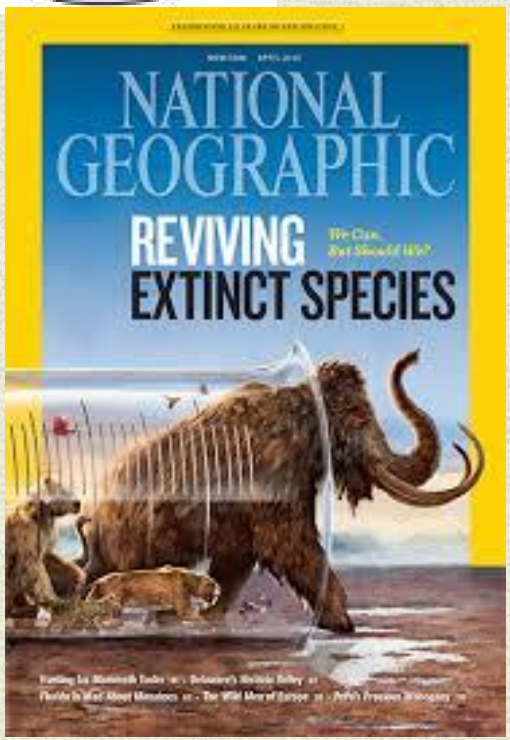
9 cases narrowed to 4 with SME review
Medium to longer term
Ag, environment focus

- Cyberplasm
- Dextinction
- Biomining
- N-fixation



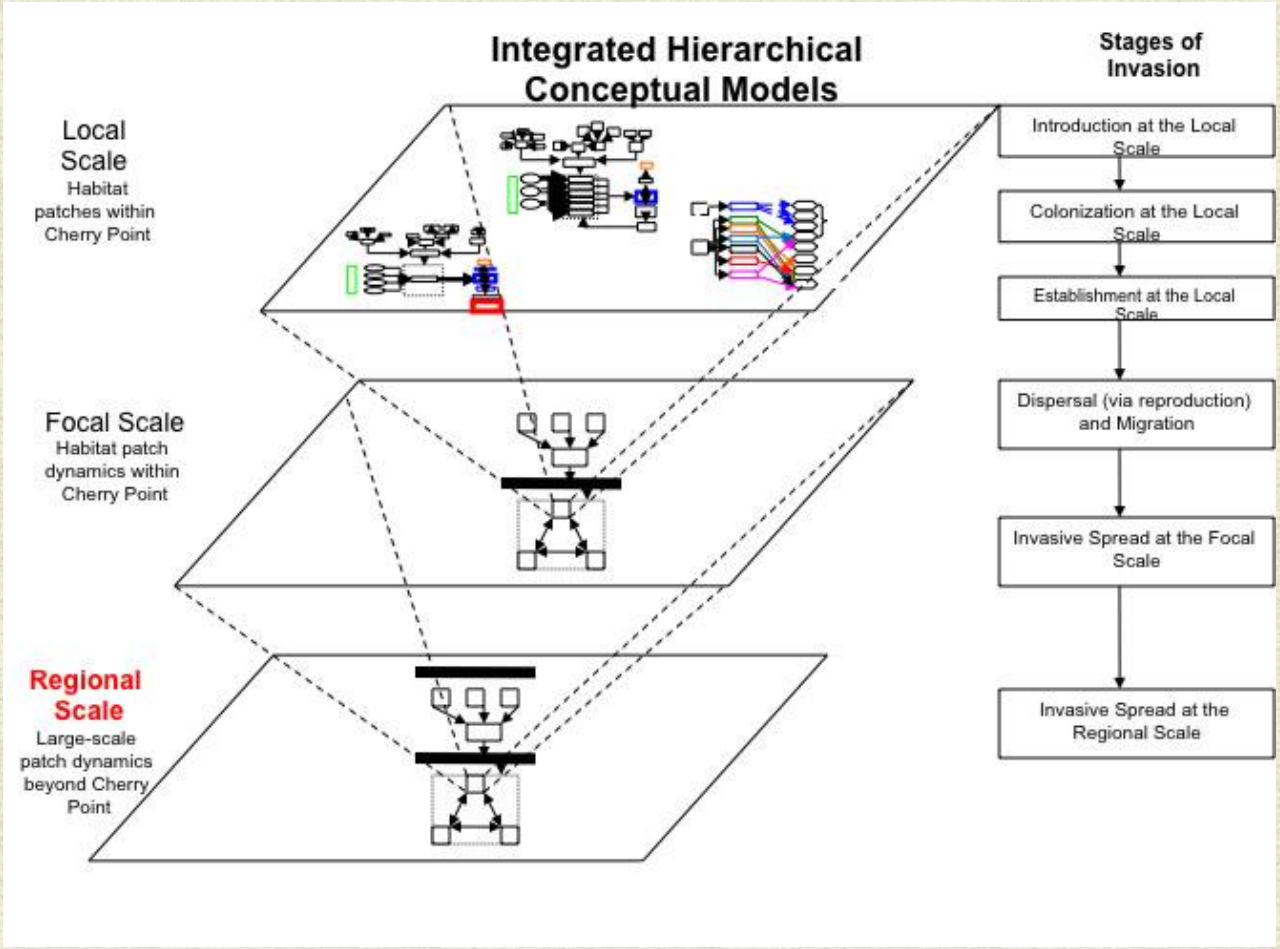






Situate New Systems Risk Analysis into Action Oriented Governance

PRA approaches



(Wu et al. invasive species RA)

Risk Analysis, Vol. 30, No. 4, 2010 DOI: 10.1111/j.1539-6924.2010.01401.x

Probabilistic Risk Analysis and Terrorism Risk

Barry Charles Ezell,[1] Steven P. Bennett,[2] Detlof von Winterfeldt,[3] John Sokolowski,[1] and Andrew J. Collins[1]

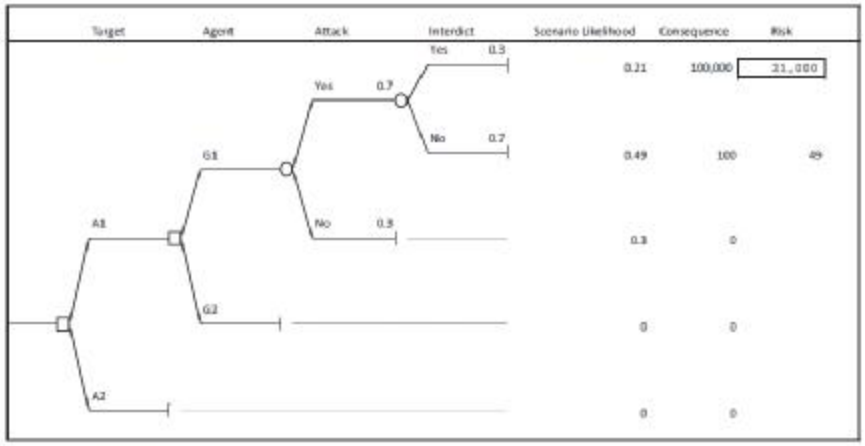


Fig. 4. Notional bioterrorism decision tree.

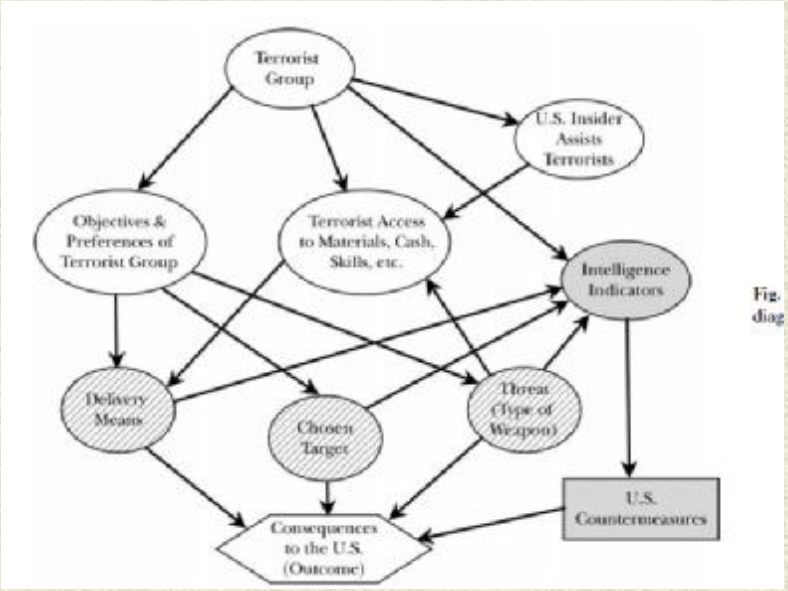


Fig.
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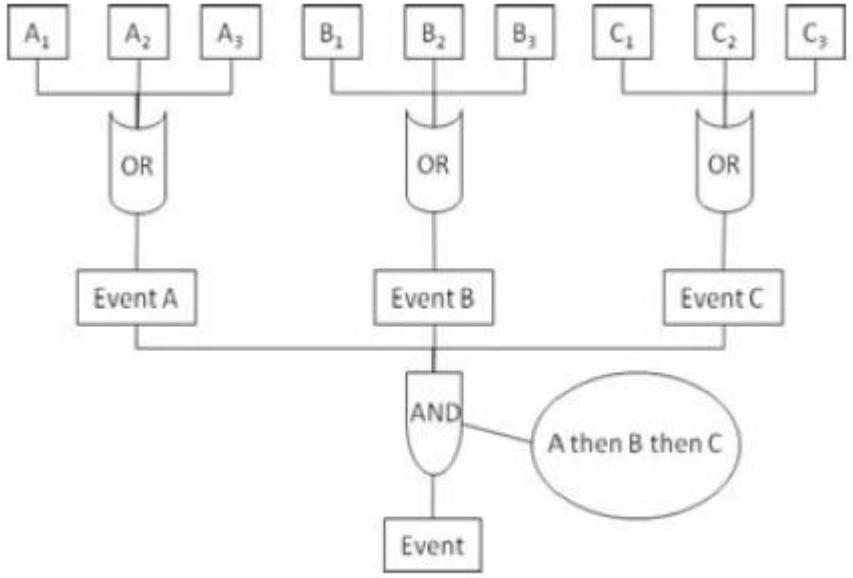


Fig. 5. Generic fault tree.

RA system approaches

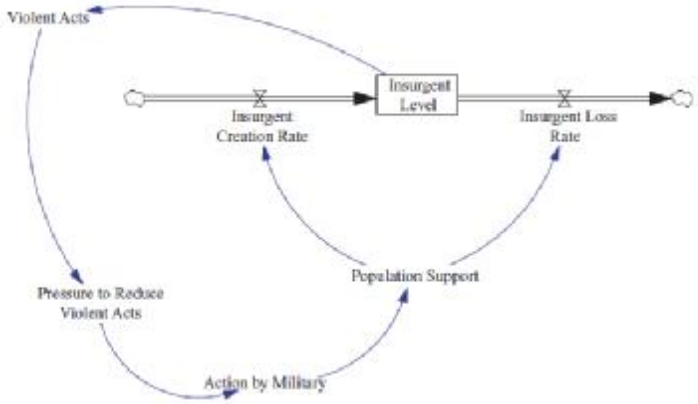
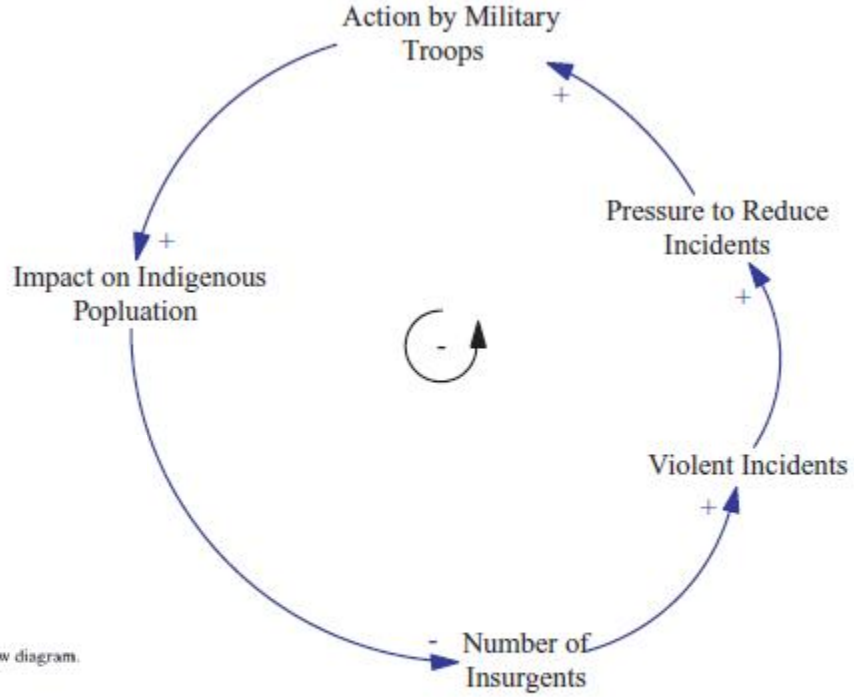


Fig. 8. Insurgent stock and flow diagram.



urgency causal loop diagram.

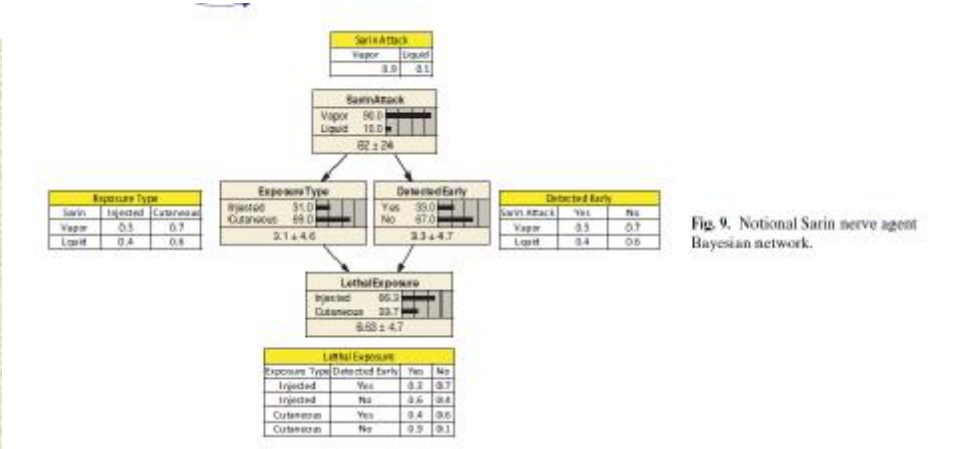
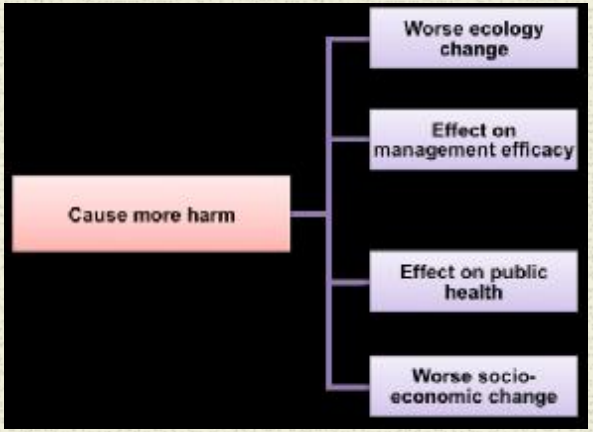


Fig. 9. Notional Sarin nerve agent Bayesian network.

Biotechnology

- Most advanced technological system of 21st century
- Investing billions in technology
- Least advanced in using ALREADY standard academic RA approaches
- Investing a couple million in biotech RA

A New Rising above the gathering storm?
U.S. is falling behind in New approaches Match uncertainty, complexity, ambiguity

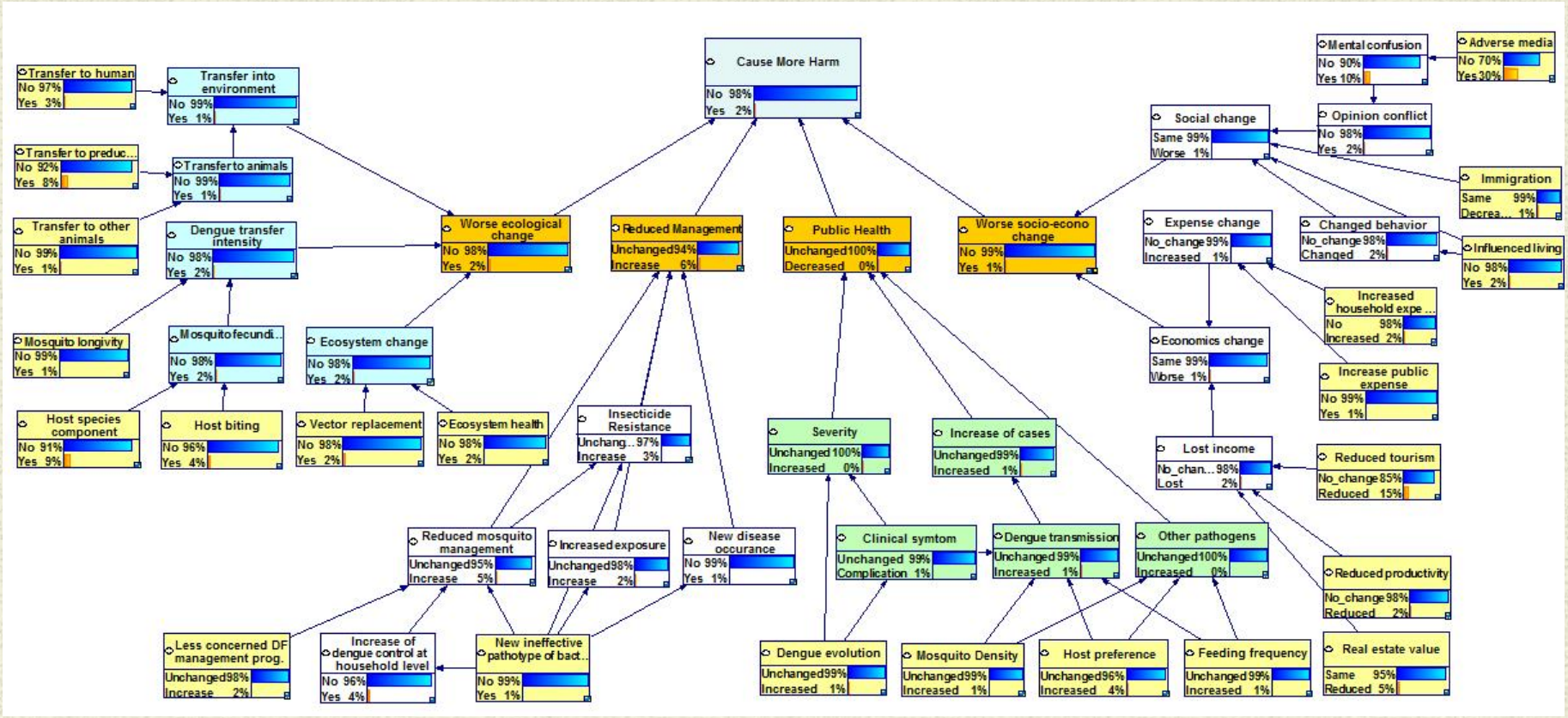


Vietnam Eliminate Dengue Project

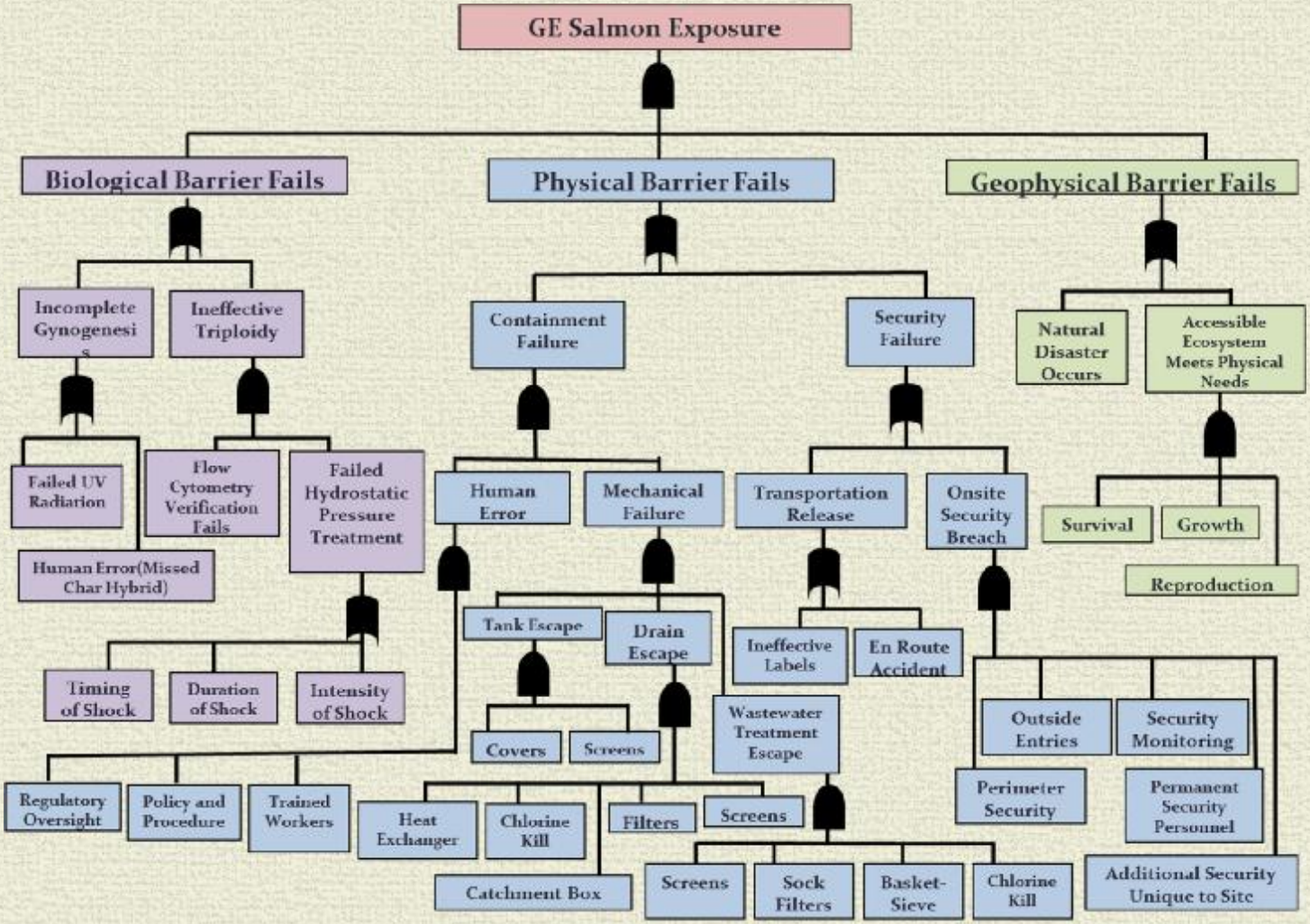
Risk Assessment of the Pilot Release of *Aedes aegypti* mosquitoes containing *Wolbachia*

Hanoi September 2011

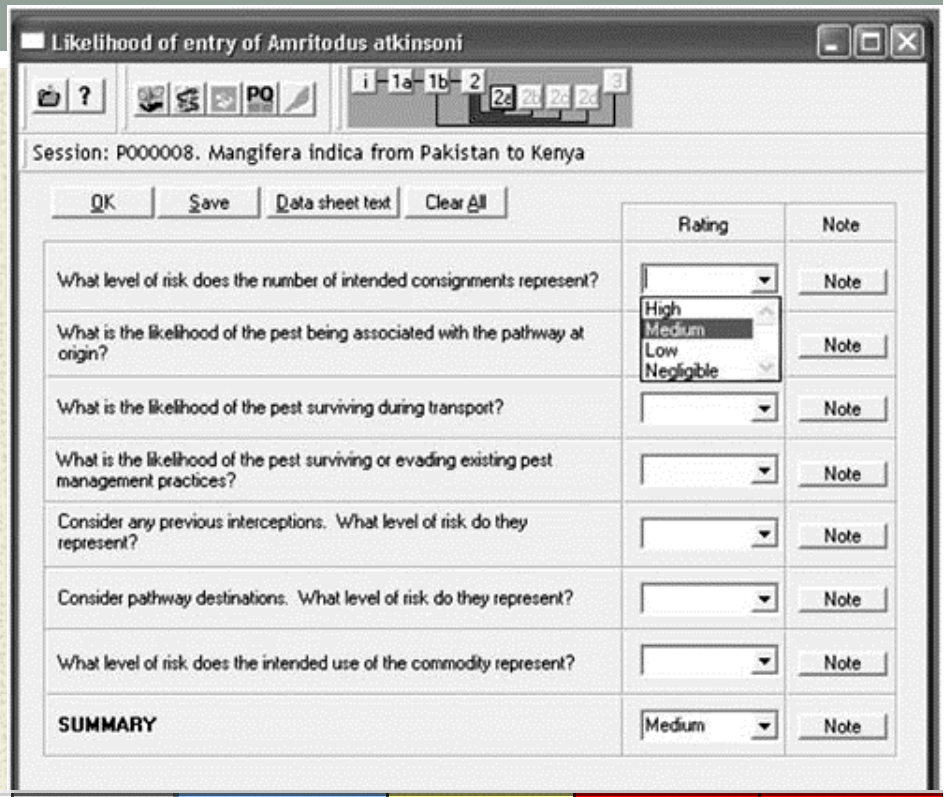
Bayesian Belief Networks and Expert Elicitation



We have the tools now to do better (students in PA 5741)



Basic Starting Point for SB?
Pest Risk Assessment

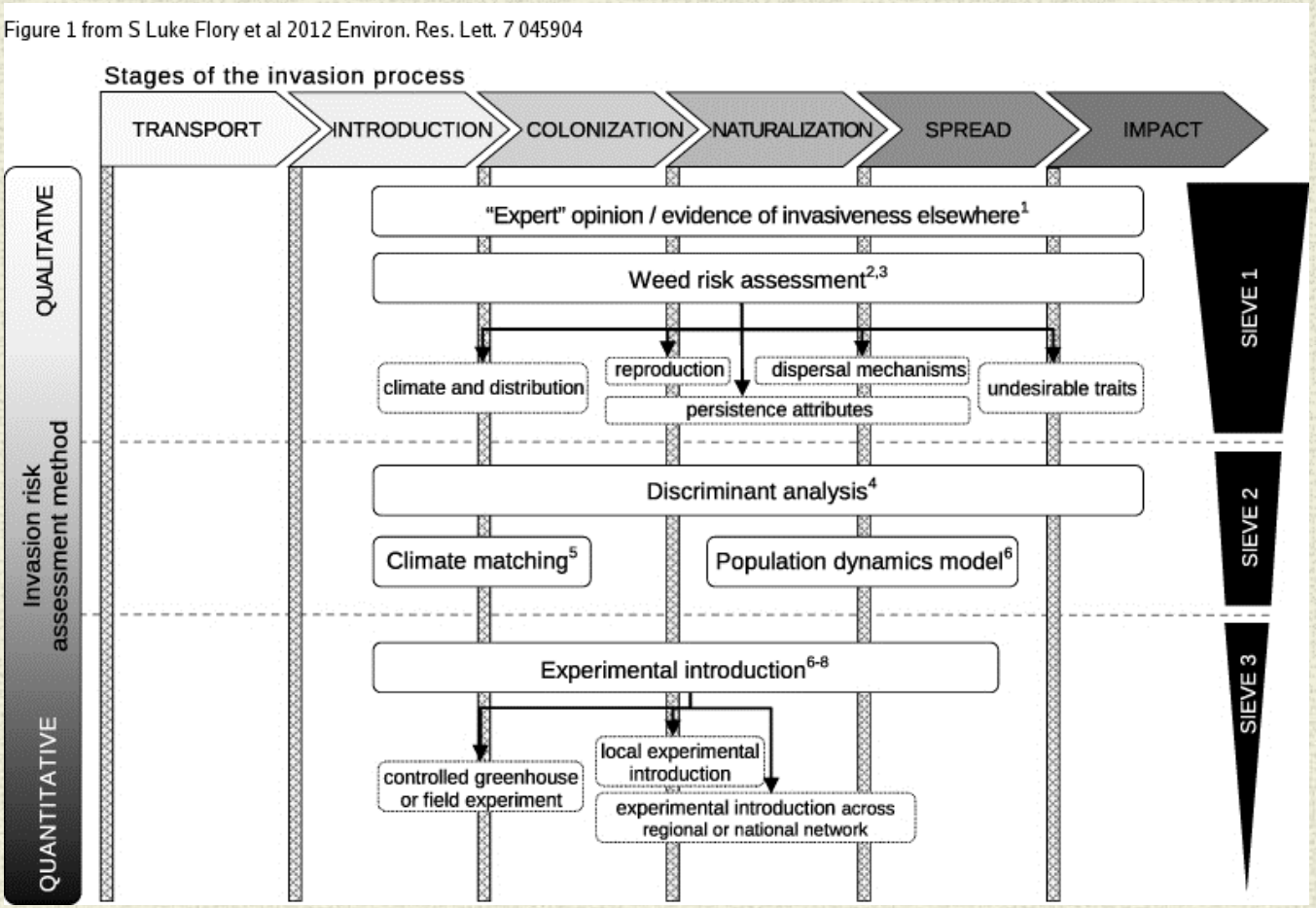


Likelihood of Escape and Establishment	Very Low	Low	Medium	High
High	PPC-1	PPC-2	PPC-3	PPC-3
Med	PPC-1	PPC-1	PPC-2	PPC-3
Low	BASIC	BASIC	PPC-1	PPC-2
Very Low	No containment required	BASIC	PPC-1	PPC-1

Consequence

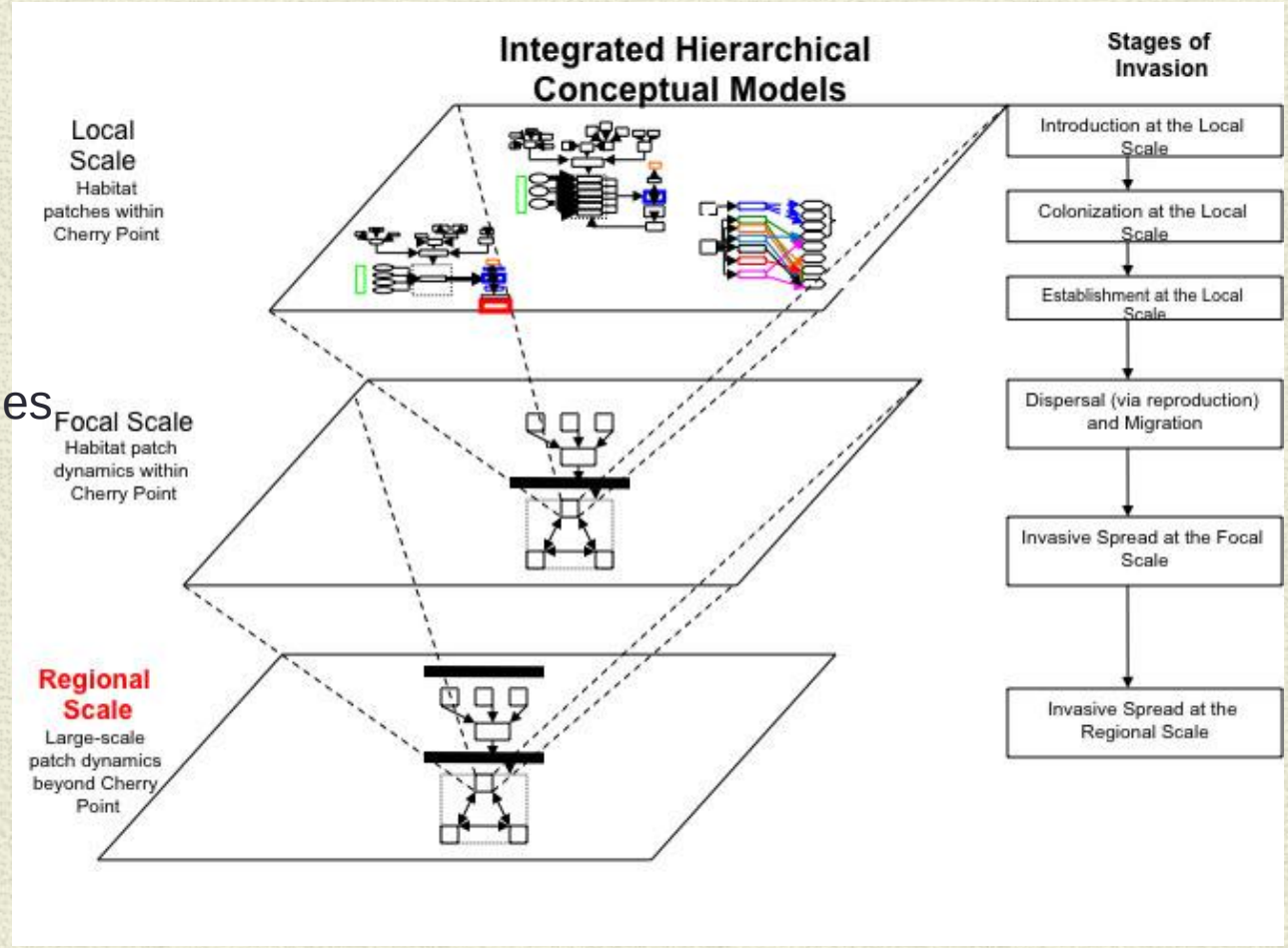
Then incorporate PRA into broader life cycle context
Use Delphi process for select syn bio applications

Figure 1 from S Luke Flory et al 2012 Environ. Res. Lett. 7 045904



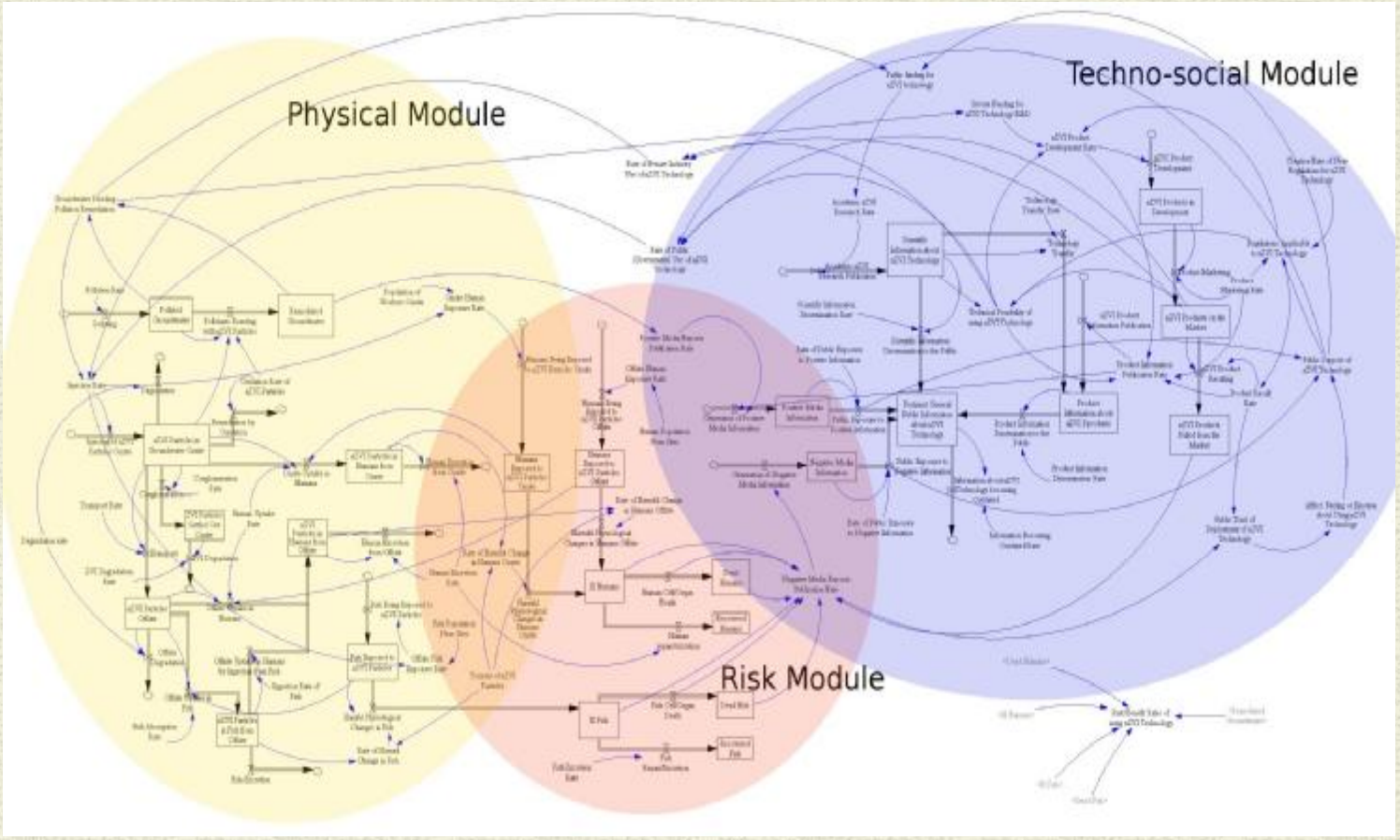
Situate New Systems Risk Analysis into Action Oriented Governance

NeSRA approaches

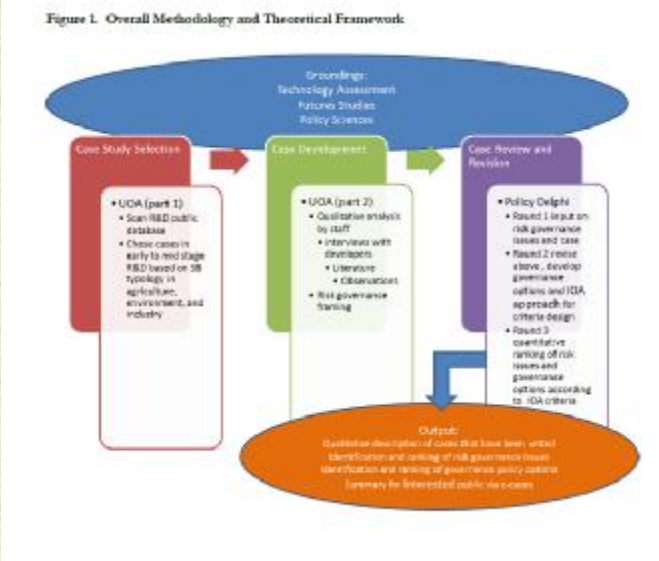


(Wu et al. invasive species RA)

Systems Mapping—Socio-Ecological Technological Systems



R. Johnson (thesis 2010) and, Johnson and Kuzma (in prep.)



Sloan Risk Governance Study

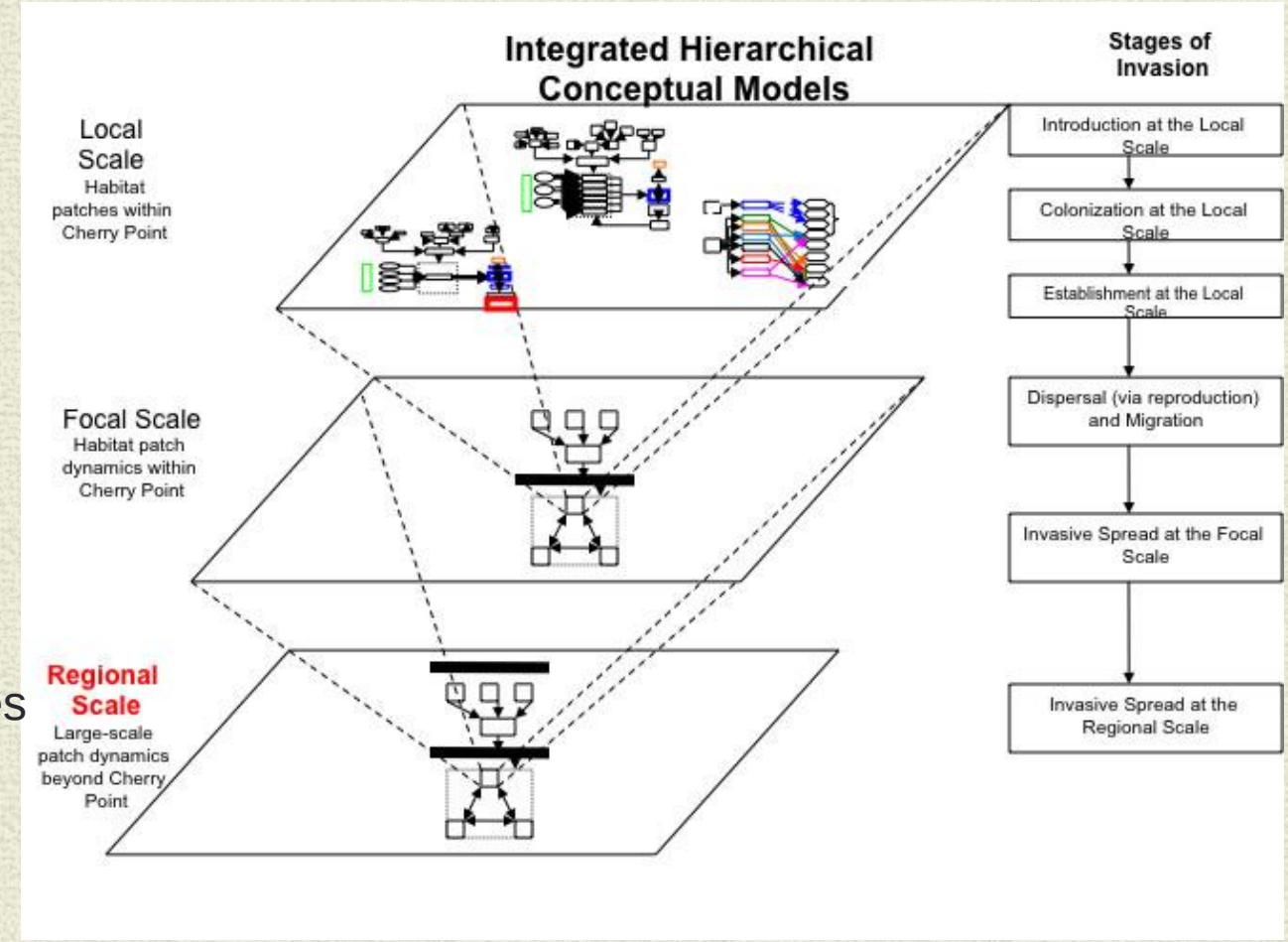
- Design of stage 2 and/or workshop

- Move towards NeSRA
- Present SMEs with
  - basic pest risk models
  - fault trees
  - systems maps
  - policy options (decision trees)
- Revise, add
- Identify information needs
- Critieria to evaluate
- Add detail to case studies

- Stage 3, refine above, reflect on A-OG process (policy Delphi)

Situate New Systems Risk Analysis into Action Oriented Governance

AO-G approaches



(Wu et al. invasive species RA)

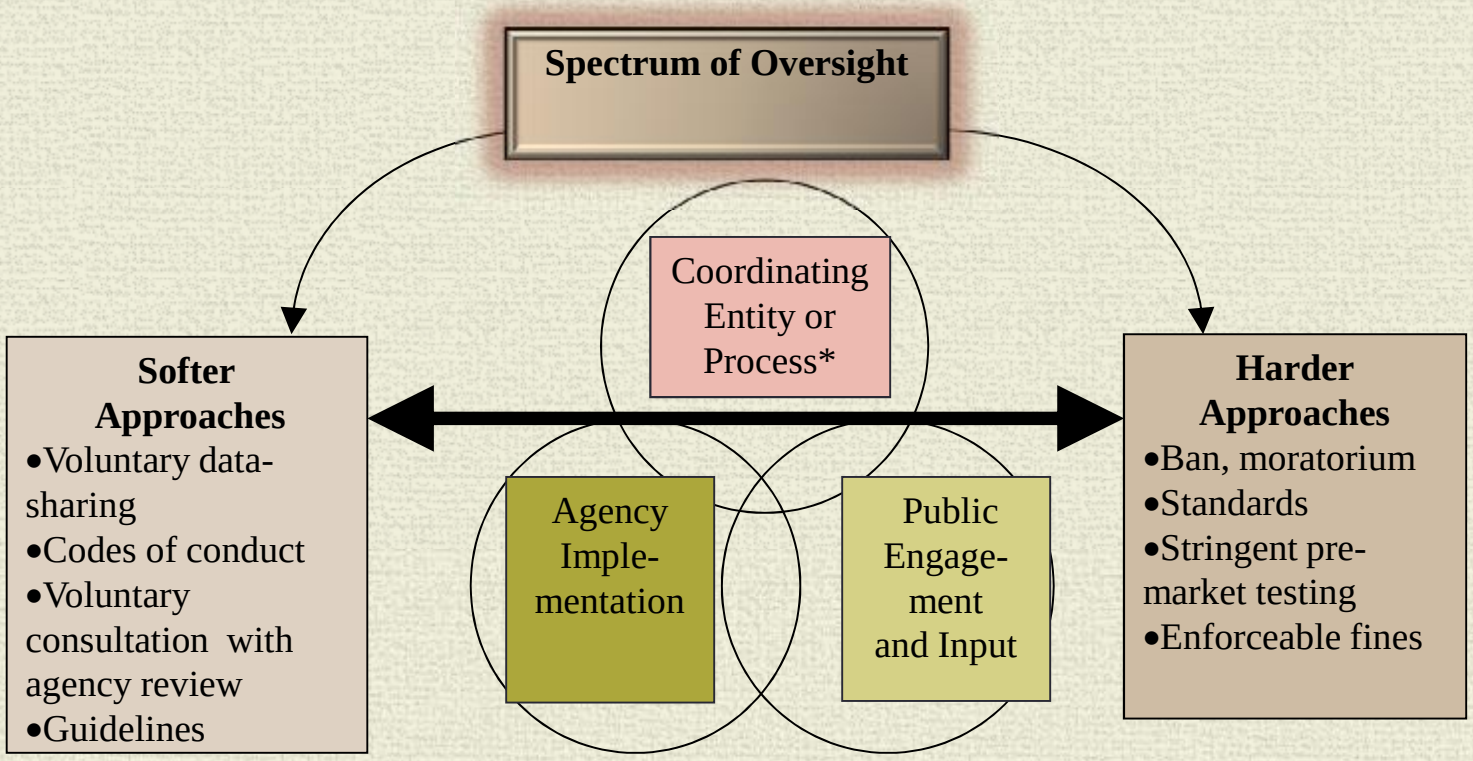
J Nanopart Res (2011) 13:1345–1371
DOI 10.1007/s11051-011-0233-2

SPECIAL FOCUS: GOVERNANCE OF NANOBIOTECHNOLOGY

Recommendations for oversight of nanobiotechnology: dynamic oversight for complex and convergent technology

Gurumurthy Ramachandran · Susan M. Wolf · Jordan Paradise · Jennifer Kuzma · Ralph Hall · Efrosini Kokkoli · Leili Fatehi

Vision of Dynamic Oversight (A-OG)
Incorporate NeSRA into A-OG framework

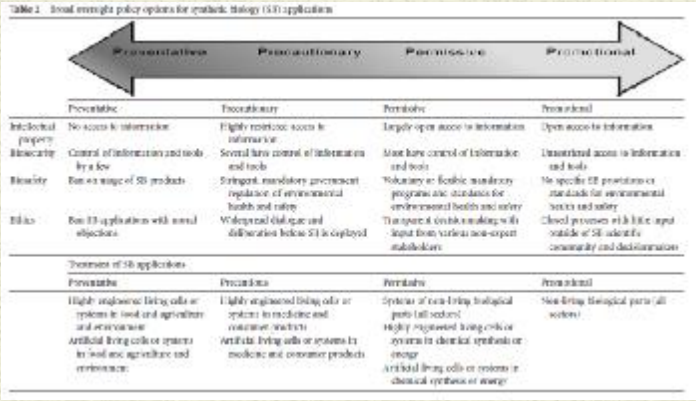


* with citizen, governmental, academic, industry, tribal, and NGO representation

For every application of SB?

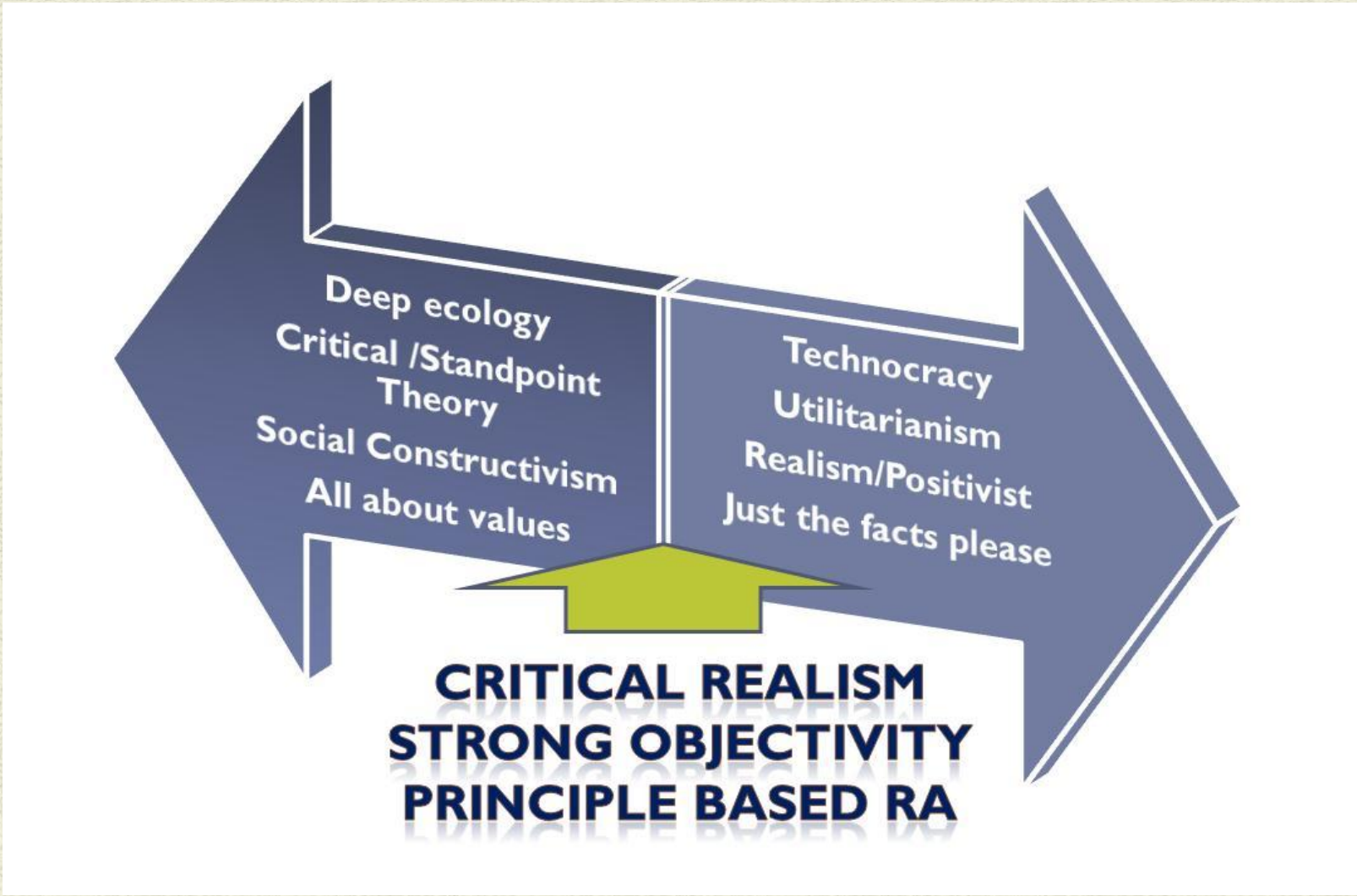
- Our policy Delphi--$180K
- Plus NewSRA, plus integrating into AO-G--$1 M?

- Prioritizing process in our Delphi (narrowed 9 to 4)



- Process for sub-categories of SB?
- Individual SB tech development projects?
- Mixture of both at first?

Middle ground (NewSRA, AO-G)?



Three huge challenges-barriers

- Elite Disciplinary Biases
  - Only the technological developers and experts know what is science-based and appropriate
- Political will
  - There are the legal and regulatory tools to include a broader notion of harms (NEPA, EIS, E.O. 12866, CBA)
  - There is NOT the political will
- Capacity
  - New risk analysis will require greater capacity within organizations that convene, conduct, and research the processes.
  - Lack of funding to conduct policy science experiments with governance and new risk analysis approaches
- Elephants in the room…but
- If any set of technologies would justify this commitment, it would be synthetic biology.
  - This is “new life”, redesigning life, controlling species in the environment, bringing back species to life.

Summary Points

- We are at a unique place of technological development and convergence that warrants a new paradigm
  - SB may be an incremental or revolutionary depending on the application, sub-technologies used, purpose, and sector applied.
- However, we need to move beyond the entrenched debates of "precaution vs. promotion", "luddites vs. technology advocates", "nothing new for risk vs. totally new and scary",
  - SB gives us an opportunity to work together across sectors, biases, and expertise areas to explore new risk analysis and governance options.
- Innovation in the area of governance is needed, with particular attention to broader risks (harms) and SET systems.
- What that new paradigm should be is debatable and underexplored, but NeSRA and AO-G form two possibilities that can be integrated/
  - For NeSRA, draw upon RA literature
  - For AO-G, draw upon governance studies literature (STS and STP, etc.)

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  - Project Asst.: Sharon Stauffer
- All Delphi participants!

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